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Proposed Re-evaluation Decision PRVD2016-09

Iprodione

(publié aussi en français)

17 March 2016

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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Canada

ISSN: 1925-0959 (print)
1925-0967 (online)

Catalogue number: H113-27/2016-9E (print)
H113-27/2016-9E-PDF (PDF version)

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Overview

General Introduction

In Canada, pesticides are regulated under the *Pest Control Products Act*, administered by Health Canada's Pest Management Regulatory Agency (PMRA). All pesticides are registered (i.e. approved) if a rigorous scientific assessment indicates that the health and environmental risks are acceptable and the products have value. The *Pest Control Products Act* also contains provisions for post-market reviews of registered pesticides namely, re-evaluation and special reviews, to assess whether pesticides continue to meet Health Canada's health and environmental standards, and whether they can continue to be used in Canada.

As part of the decision making process, before making a final decision, the PMRA consults with the members of the public and other interested stakeholders on all proposed major decisions such as new registrations, re-evaluations and special reviews. The PMRA encourages the public and stakeholders to participate in the consultation process. The proposed decisions are made based on the information available at the time, and the PMRA will consider the comments and information received during consultation using a science-based approach before making a final decision. The final decision will be published on the Pesticides and Pest Management portion of Health Canada's website and it will include a summary of the comments received during the consultation and PMRA's responses to the comments.

The registration status of products and conditions of use of pesticide products on the market are not impacted by proposed re-evaluation or special review decisions. This may be the case only when final decisions are made. However, at any point during the re-evaluation or special review of a pesticide, the *Pest Control Products Act* allows the PMRA to cancel or amend the registration of registered pest control products, if there are reasonable grounds to believe this is necessary to deal with a situation that endangers human health or safety or the environment.

Proposed Re-evaluation Decision for Iprodione

An evaluation of available scientific information has determined that under the currently labelled conditions of use, the human health risks estimated for iprodione do not meet current standards. Therefore, the cancellation of all iprodione usesis proposed at this time. Consideration of any additional data/information submitted during the consultation period to further refine the health risk assessment may or may not result in a change to this proposal.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for iprodione and presents the reasons for the proposed re-evaluation decision.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides details on the risk assessments conducted for iprodione.

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

The PMRA will accept written comments and data/information up to 90 days from the date of publication of this document. Please forward all comments on this proposal to Publications (see contact information on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[2] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration. The Act also requires that products have value[3] when used according to the label directions. Requirements of registration may include precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (for example, children) and organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at www.healthcanada.gc.ca/pmra.

Before making a re-evaluation decision on iprodione, the PMRA will consider all comments/information received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision document[4] on iprodione, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation part of this consultation document.

What is Iprodione?

Iprodione is a contact fungicide with protective and curative action. It works by inhibiting the germination of spores and growth of fungal mycelium. In Canada, it is used to control a broad range of fungal pathogens on a wide variety of greenhouse, orchard and field crops, ornamentals and on turf. It is applied using ground and aerial application equipment by farmers, greenhouse and nursery workers, and professional applicators.

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[2] "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

[3] "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's *(a)* efficacy; *(b)* effect on host organisms in connection with which it is intended to be used; and *(c)* health, safety and environmental benefits and social and economic impact".

[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Iprodione Affect Human Health?

Risk concerns were identified from food and drinking water exposure to iprodione.

Potential exposure to iprodione may occur through the diet (food and water), when handling and applying products containing iprodione or by entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

In laboratory animals, iprodione was of slight acute toxicity by the oral route while dermal and inhalation exposure resulted in low acute toxicity. It was a mild eye irritant but not irritating to the skin. Iprodione did not produce an allergic skin reaction.

Registrant–supplied short, and long term (lifetime) animal toxicity tests, as well as numerous peer–reviewed studies from the published scientific literature were assessed for the potential of iprodione to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints used for risk assessment included changes in weights of some endocrine organs and impaired male sexual development. An increased incidence in several tumor types was observed in rats and mice following long-term dosing with iprodione. There was no indication that the young were more sensitive than the adult animal. The risk assessment takes these and any other potential effects into account in determining the allowable level of human exposure to iprodione.

Residues in Water and Food

Dietary risks from food and water are of concern. In order to address these concerns, all registered uses considered in the dietary exposure and risk assessment are proposed for cancellation unless there is information/data submitted during the consultation period that would alter the risk assessment.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). For the cancer assessment, a lifetime cancer risk that is less than one-in-a-million (1×10^{-6}) is generally considered an acceptable risk for the general population when exposure occurs through pesticide residues in/on food and drinking water, and to otherwise unintentionally exposed persons.

Potential exposure was estimated from residues of iprodione and relevant metabolites in both treated crops and drinking water. Exposure to different subpopulations, including children and women of reproductive age, were considered. Food residue estimates were based mostly on surveillance data and included percent crop treated information and chemical-specific processing factors when available. Drinking water estimated environmental concentrations (EECs) were based on the modelling of iprodione residues in groundwater. Different EECs were determined using the typical use rates for turf, orchard or canola applications.

Acute and chronic (non-cancer) exposures from iprodione in food and drinking water were below the acute reference dose (ARfD) and ADI for most population groups at the use rates assessed. However, the cancer risk exceeded 1×10^{-6} for the general population for all use rates assessed and is of concern. The estimated cancer risks ranged from 3×10^{-6} to 5×10^{-5}. Exposure from drinking water was the major risk contributor in the cancer assessment. Exposure from food commodities was also a significant contributor in the assessment with an estimated cancer risk of 1×10^{-6}. The exposure and risk from food commodities is largely attributed to residues in/on imported South American stone fruits.

Canadian MRLs for iprodione are currently specified for a wide range of commodities. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. The current MRLs for iprodione are listed in Appendix VII of the Science Evaluation. The revocation of all established MRLs is proposed to reduce dietary risk and to align with the proposed decision to cancel all registered uses in Canada.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern.

There are currently no registered residential uses of iprodione; as such a risk assessment for a residential handler was not required.

Agricultural application of iprodione may result in spray drift. Studies that sampled the air in agricultural areas in the United States and Europe during the spray season indicate that iprodione can be present in ambient air. Risk estimates based on the highest level of iprodione measured in the air resulted in non-cancer and cancer risk assessments that are not of concern.

Agricultural application of iprodione may result in iprodione residues in homes. Studies that sampled dust, floors, and clothing indicate that there is potential for incidental exposure for children. Risk estimates based on the highest level of iprodione measured in homes resulted in non-cancer and cancer risk assessments that are not of concern.

Commercial application of iprodione to golf courses could lead to exposure for people golfing. Risk estimates for golfers resulted in non-cancer and cancer risk assessments that are not of concern.

Aggregate risk estimates where exposure from food and drinking water are combined with possible bystander exposure were not conducted due to cancer concerns with food and drinking water.

A cumulative assessment was not required at this time.

Occupational Risk to Mixer/Loader/Applicator and Post-Application Workers

Occupational (mixer/loader/applicator) risks are of concern for some uses when products are used according to the current label directions, but can be mitigated.

Risks for farmers and workers who mix, load and apply iprodione for agricultural crops (fruits and vegetables, ornamentals, canola, alfalfa and turf) are of concern for some scenarios. However, they can be effectively mitigated using additional personal protective clothing and engineering controls (such as water soluble packaging, protective headgear and/or closed cabs).

Risks for farmers and workers who treat canola and mustard seed or potato seed pieces are of concern for some scenarios when used according to the current label directions. However, they can be effectively mitigated using additional personal protective clothing and engineering controls (such as closed mix, load and transfer systems).

Adequate data were not available to assess exposure from the use of iprodione in commercial garlic bulb dipping facilities, or in greenhouses when using hand-held mistblowers or foggers.

Occupational post-application risks are of concern for most uses when products are used according to the current label directions, and mitigation may not be agronomically feasible.

Post-application occupational risk assessments consider exposure to workers entering treated sites in agriculture and other scenarios. Based on the precautions and directions for use on the current product labels, most post-application risks to workers performing activities such as thinning, pruning and harvesting of crops are of concern. Occupational post-application risks can be mitigated by revising the restricted entry intervals (REIs). The REIs proposed to mitigate post application risk range from 1 to 137 days and therefore, may not be agronomically feasible.

Post-application risk may also be of concern to workers who plant treated seeds (such as canola, mustard, and carrot). However, they can be effectively mitigated using additional engineering controls (such as closed cab planting).

Environmental Considerations

What Happens When Iprodione Is Introduced Into the Environment?

When used according to label directions, iprodione is not expected to pose an unacceptable risk to the environment.

When iprodione is released into the environment some of it can be found in soil and surface water. In the terrestrial environment, iprodione is expected to break down in the presence of soil microbes and is not very persistent. Depending on the soil type, it takes microbes from 2 weeks to 6 months to break down half of the iprodione present in soil. In the aquatic environment, iprodione is also broken down by microbes, but much more rapidly than in soil. When iprodione is applied to soil it is not expected to leach into groundwater, but under sandy soil conditions it has the potential to move downward through the soil profile and potentially enter groundwater. Iprodione has not been detected in surface or groundwater; however, Canadian monitoring data for iprodione is limited. Iprodione is not expected to enter the atmosphere and be transported long distances from where it is used. Iprodione is not likely to accumulate in the tissues of organisms such as fish.

Iprodione is found to be toxic to bees, beneficial arthropods, birds, small wild mammals and aquatic organisms when exposed to high enough concentrations. Consequently, if iprodione is used at labelled application rates without any risk reduction measures, it may cause adverse effects in the organisms listed above. Therefore, risk mitigation measures, in the form of use restrictions and precautionary label statements would minimize exposure and mitigate potential risks. The risk to aquatic organisms would be mitigated with spray buffer zones and recommendations on the label to reduce runoff from fields. Hazard statements would inform users of the toxicity of iprodione to beneficial insects and mammals.

Value Considerations

What is the Value of Iprodione?

Iprodione is used to control several economically important fungal diseases on a wide variety of food and non-food sites, including significant uses on large crops like canola and intensively managed sites such as turf.

Iprodione is registered in Canada for the control of many economically important fungal diseases on several field, orchard, nursery and greenhouse crops and ornamentals, conifer seedlings and turf (in other words, 24 crops, 53 ornamentals and turf against 28 fungal pathogens). Particularly important uses of iprodione include: foliar treatments to control Sclerotinia stem rot and *Alternaria* black spot on canola; and brown and Fusarium patch, leaf spots, snow moulds and dollar spot on turf.

Iprodione is effective as a protective and curative fungicide. Because of these properties, it can be used as a tank-mix partner or as a rotational fungicide with fungicides from other chemical groups in an integrated pest management (IPM) program to manage development of resistance in pathogens.

Measures to Minimize Risk

The PMRA has assessed the available information and concluded that the use of iprodione and associated end-use products in accordance with the label poses potential risks of concern to human health. Specifically, potential health risk concerns were identified from exposure to iprodione in food and drinking water and from exposure to occupational workers under certain use scenarios. Therefore, the PMRA is proposing to cancel all uses of iprodione in Canada.

What Additional Scientific Information Is Being Requested?

As the PMRA is proposing cancellation of all uses of iprodione, no additional data will be required under section 12 of the *Pest Control Products Act*.

Next Steps

Before making a final re-evaluation decision on iprodione, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Science Evaluation

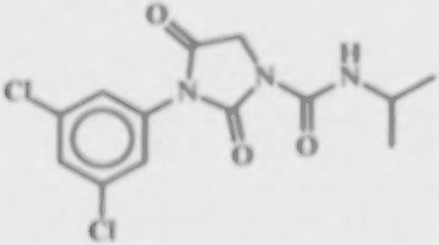
1.0 Introduction

Iprodione is a contact fungicide with protective and curative action that inhibits germination of spores and growth of fungal mycelium. It is a dicarboximide fungicide classified in Group 2 by the Fungicide Resistance Action Committee (FRAC). The mode of action (MoA) of iprodione has not been fully characterized, but recent studies suggest that it interferes with the fungal osmotic signal transduction pathway consisting of histidine kinase and mitogen-activated protein (MAP) kinase cascades.

The registrants and primary data providers for iprodione technical grade active ingredient (TGAI), FMC Corporation and Adama Agricultural Solutions Inc., confirmed their intent to provide continued support for all iprodione uses during the re-evaluation. As of 27 April 2015 there are 12 Commercial Class products formulated with iprodione registered in Canada.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name		Iprodione
Function		Fungicide
Chemical Family		Dicarboximide
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	3-(3,5-dichlorophenyl)-N-isopropyl-2,4-dioxo-imidazolidine carboxamide
2	**Chemical Abstracts Service (CAS)**	3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine carboxamide
CAS Registry Number		36734-19-7
Molecular Formula		$C_{13}H_{13}Cl_2N_3O_3$
Structural Formula		

Molecular Weight 330.2

Registration Number	Purity of the Technical Grade Active Ingredient
20267	98.0% nominal (limits: 96.0-100%)
29379	99.0% nominal (limits: 96.05-100%)
31892	98.0% nominal (limits: 96.0-100%)

Identity of relevant impurities of human health or environmental concern:

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	5×10^{-4} mPa
Ultraviolet (UV)/visible spectrum	Not expected to absorb UV at $\lambda > 290$ nm
Solubility in water at 20°C	13 mg/L
n-Octanol/water partition coefficient (Log K_{ow})	Log K_{ow}=3.0 at pH3 & pH5
Dissociation constant	Not applicable (iprodione does not dissociate)

2.3 Description of Registered Iprodione Uses

Appendix I lists all iprodione products that are registered under the authority of the *Pest Control Products Act* and Appendix II lists all of the uses of Commercial Class products for which iprodione is currently registered as of 27 April 2015. All uses were supported by the registrant at the time of initiation of re-evaluation and were therefore considered in the health and environmental risk assessments of iprodione.

Uses of iprodione belong to the following use-site categories (USC): greenhouse food crops, greenhouse non-food crops, industrial oil seed crops and fibre crops, seed treatments for food and feed, terrestrial feed crops, terrestrial food crops, outdoor ornamentals and turf.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for iprodione was conducted. In addition, results of several toxicology studies reported in other regulatory authority documentation were considered. The scientific quality of the data and the database in general is considered adequate to define the majority of the toxic effects that may result from exposure to iprodione. The purity of iprodione used in the toxicity studies ranged from 93.5-100%, with purities not reported for a small number of studies. Observed effects were consistent among studies and the ranges of purities were not considered to have an impact on the observed results.

In studies in rats, radiolabelled iprodione was readily absorbed after a single oral dose. After administration of a low dose, blood levels peaked at 2-4 hrs, while high-dose blood levels peaked at approximately 6 hrs. At 4 days post-dosing, tissue samples contained low levels of radioactivity indicating rapid excretion. At 7 days post-dosing, the liver, intestines and skin were the organs that contained the highest levels of radioactivity. Iprodione was extensively metabolized regardless of dose. Iprodione biotransformation included hydroxylation of the aromatic ring, dealkylation and degradation of the isopropylcarbamoyl chain and rearrangement followed by cleavage of the hydantoin moiety. Molecular rearrangement also results in iprodione isomers and formation of intermediate metabolites. The urine contained predominantly RP32490 and RP36114 as well as some unchanged iprodione, RP36112, RP36115, RP36116, RP36118 and RP36119. The faeces contained the same metabolites as the urine, as well as RP25040 and RP30228. The most common compounds in the faeces included unchanged iprodione, RP36115/36119 and RP36114, with up to 45% of the radioactivity uncharacterized. Urinary excretion was more prominent at low doses, while the fecal route played a greater role following high-dose exposure. More unchanged iprodione was excreted by females than males and with higher administered doses. Elimination occurred more slowly in males than in females.

In acute toxicity studies, iprodione caused slight oral toxicity in all species tested. Clinical signs from the acute oral studies included decreases in muscular tension, depression, slow respiration, dyspnea and systemic paralysis (paralysis progressed in order of hind legs, forelegs and then whole body). Low acute toxicity was demonstrated from the dermal route of exposure in rats and rabbits and from the inhalation route of exposure in rats. Iprodione was a mild eye irritant in rabbits but was not irritating to rabbit skin. It was not a dermal sensitizer in guinea pigs via the Buehler method.

Repeat-dose oral toxicity studies performed on mice, rats and dogs identified the adrenal, liver and reproductive organs as target organs. Dogs and rats were the most sensitive to adrenal effects. Enlarged cells of the zona glomerulus and microscopic lesions (vacuolation of both the zona fasciculata and zona reticularis) were regularly observed. Hypertrophy of adrenal zona fasciculata cells, increased adrenal weight and more extensive adrenal vacuolation were observed in animals exposed to higher doses of iprodione. The adrenal effects were more pronounced and occurred at lower doses in longer-term studies.

Liver effects consisted of increased weights, increased enzyme levels, hepatocyte hypertrophy and vacuolation in rodents. With longer-term dosing, mice exhibited additional hepatic effects including foci, necrosis, multi-nucleated hepatocytes, pigmented macrophages and erythrophagocytosis. Increased liver weights and hepatic cord atrophy were noted in dogs administered high doses of iprodione in the diet for one year.

Effects on male reproductive organs were consistently observed in the repeat-dose dietary studies, with rats and dogs being the most sensitive species. Prostate weights were reduced in dogs following administration of low doses of iprodione; at a high dose, hypogonadism was observed. Effects in male rats consisted of decreases in size and/or weights of the testes, prostate and seminal vesicles, as well as increased incidences of prostatic atrophy and reduced secretion from the seminal vesicles. At higher doses, male rats exhibited decreased, absent or abnormal epididymal spermatozoa, hyposecretion of the prostate, atrophy of the seminiferous tubule and Leydig cell hyperplasia. With long-term dosing, effects progressed to interstitial cell tumours (Leydig cell tumors), accompanied by increased testes and epididymal weights. In mice, effects were noted on the weights and pathology of the testes. Partial or total arrest of spermatogenesis was noted in mice at very high doses. Long-term dosing in mice resulted in Leydig cell hypertrophy, hyperplasia and prostatic cysts, as well as effects on epididymal weights and pathology.

The reproductive organs of female rats and mice were affected in short and long-term dietary studies. Uterine effects included reduced organ weight, increased incidence of atrophy, and changes in the thickness of the epithelium in both species; hyperplasia was noted in mice and dilation, polyps and cysts were noted in rats. Ovarian effects in both species included alterations in organ weights and reduced numbers or absent corpora lutea. An increased incidence of ovarian cysts, atrophy and luteinisation of the interstitial cells was observed in mice. Ovarian tubular hyperplasia was also increased in rats. In one two-year rat study, ovarian histopathology was not fully assessed in the low- and mid-dose groups. In order to fully characterize the effect of iprodione on this organ in this study, a full histopathological analysis in the low- and mid-dose groups would be required.

Other effects observed in the iprodione database which were common to all species included decrease in body weight, body weight gain and food consumption. Clinical signs of toxicity and increases in mortality were observed in rats and mice. Mice-only effects included granulomatous lesions in several tissues, extramedullary hematopoiesis, increased pigmentation of nose and cecum, dilated/cystic glands of stomach, vacuolar changes of the pancreas, splenic hemosiderosis and hyperkeratosis of the forestomach. Decreases in brain and kidney weights and absent cytoplasmic vacuolation were also observed in mice. Effects occurring solely in dogs included decreases in red blood cell parameters.

No adverse effects were noted at any dose level up to and including the limit dose (1000 mg/kg bw/day) in the repeat dose dermal rabbit study. It is important to note that while organ weights and gross pathology assessments were conducted on testes/epididymides and ovaries, histopathology assessments of these tissues were not undertaken.

A standard battery of genotoxicity studies, including an *in vivo* mouse micronucleus study, was available for iprodione. The results of these studies did not suggest that iprodione was genotoxic.

There were four dietary carcinogenicity studies conducted in rodents (two in mice, two in rats) in the iprodione database. In both dietary carcinogenicity studies in mice, an increase in hepatocellular tumours was noted in both sexes at the high dose. The increase was observed for both hepatocellular adenomas and carcinomas in one study but only for adenomas in the other. A mode of action was proposed for liver tumour development. Although liver study findings showed increased microsomal enzyme activities, as well as increased liver cell proliferation with increasing dose, the weight of evidence was not sufficient to substantiate the proposed mode of action. One of the mouse studies also demonstrated an increased incidence of ovarian luteomas in females at the highest dose tested.

An increased incidence of testicular Leydig cell tumors was recorded in both dietary carcinogenicity studies in rats. Hormonal perturbation was proposed by the registrant as the mode of action for tumour formation. While the extent to which testosterone levels would be affected following chronic exposure remains unknown, short term mechanistic studies investigating hormone metabolism/activity (*in vivo* and *in vitro*) were available. Iprodione increased plasma luteinizing hormone, follicle-stimulating hormone and estradiol concentrations (*in vivo*) and decreased testosterone secretion *(in vitro, in vivo* and *ex vivo*). Changes in the pulsatile secretion patterns of testosterone and luteinizing hormone were noted as well. The ability of iprodione to bind to androgenic receptors was assessed, with low binding affinity observed relative to positive control.

The available studies, including data from the scientific literature, support a non-genotoxic mode of action for Leydig cell tumour development in male rats. Iprodione is postulated to alter the transport/ availability of cholesterol substrate, required for testosterone biosynthesis, into the Leydig cell mitochondria. The reduced cholesterol availability results in rapid alteration of circulating levels of testosterone and luteinizing hormone (LH) in rats after single and repeated iprodione exposures. Continued hormone perturbation leads to Leydig cell proliferation and hyperplasia, which ultimately results in Leydig cell tumours. Although hormone changes are transient, constant perturbations of the hormonal homeostatic balance of the hypothalamo-pituitary-testis axis are thought to lead to tumour formation over time. The lowest dose level at which these precursor effects was observed is 6 mg/kg bw/day.

The non-genotoxic mode of action resulting in Leydig cell tumour formation is biologically plausible; however, a threshold dose for the precursor effects has not yet been clearly established. While uncertainty remains with respect to the dose corresponding to absence of the testosterone/LH effects following chronic dosing, the small magnitude of the key changes at 6 mg/kg bw/day suggests that the point of departure is not far below this value. Additional information would be required to further characterize the point of departure for the precursor effects leading to the Leydig cell tumours in support of the proposed mode of action.

An increased incidence of uterine adenocarcinomas was observed in the most recent rat carcinogenicity study in mid- and high-dose animals. The interpretation of the results was constrained by the lack of histopathological assessment of the uterus in all animals in the low and mid-dose group, as well as the lack of historical control data for this tumour. In order to further characterize the impact of this finding, a full histopathological analysis of the uterus in the low- and mid-dose groups would be required.

There was one reproductive and four developmental toxicity studies considered in the iprodione database. The maternal effects in the gavage developmental toxicity studies in rats and rabbits consisted mainly of reductions in body weight/weight gain and food consumption. There were observations of mortality, clinical signs and reduced motor activity at higher doses. Increased resorptions were observed in rabbits at these high doses. In supplemental rat studies, high-dose effects included a reduction in implantations (with early dosing) and in litter size.

Fetal effects in the rat developmental toxicity studies included a decrease in anogenital distance, increased numbers of small fetuses and increased space between the body wall and organs. The effects were observed at a dose level with accompanying maternal toxicity. Decreased fetal weights were observed in both rats and rabbits at maternally toxic doses. At the highest doses of the rabbit developmental toxicity studies, various skeletal anomalies were observed in conjunction with significant maternal toxicity, including death.

In the 2-generation reproduction study, no information pertaining to the effect of iprodione on sperm measurements (in other words, sperm count, motility and morphology) was available. An assessment of organ weights was also not conducted in the study. Parental toxicity included decreases in body weight/gain. Additionally, there were decreases in litter size, live birth index and birth weights. Viability indices were reduced in some matings. All offspring effects were observed in the presence of parental toxicity. The effects of repeated exposure to iprodione on the onset of puberty and other sexual differentiation milestones (in other words, a full assessment of preputial separation, vaginal patency and nipple retention), were not examined in the available study.

Neurotoxicity potential was not fully addressed in the database. High doses of iprodione administered by gavage produced a number of neurotoxic signs including, but not limited to, ataxia, muscle flaccidity, altered reflex responses and paralysis. Evidence suggestive of neurotoxic effects in offspring was observed in the 2-generation reproduction study in the form of reduced mobility, hunching and/or tremors. As improper neural function can be associated with endocrine-mediated toxicity, an uncertainty exists with respect to the etiology of the observations. However, neurotoxic effects occurred at dose levels higher than those resulting in endocrine-mediated toxicity and therefore likely represented a secondary response to treatment.

A terminal metabolite of iprodione that can potentially be formed in water is 3,5-dichloroaniline (3,5-DCA). 3,5-DCA has not been tested for carcinogenicity in animal studies; however, it may have carcinogenic properties because it is a structural analog to p-chloroaniline which is carcinogenic in animals (PMRA #1819485). The carcinogenic potential of all chloroanilines is assumed to be the same as that of p-chloroaniline unless there is sufficient evidence that the chloroaniline in question is either not carcinogenic or is of a different potency than p-chloroaniline. Based on this lack of information, the cancer potency of p-chloroaniline will be used as a surrogate for 3,5-DCA.

The toxicology endpoints for use in the human health risk assessment are summarized in Table 1 of Appendix III. Results of the toxicology studies conducted on laboratory animals in support of iprodione are summarized in Table 2 of Appendix III. Chemical names of iprodione metabolites can be found in Table 3 of Appendix III.

Pest Control Products Act Hazard Characterization

For assessing risks from potential residues in the diet or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, as well as potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, pre-natal developmental toxicity studies in rats and rabbits, a multi-generation reproduction study in rats, as well as supplemental studies were available. Information on the effects of repeated exposure to iprodione on the onset of puberty and other sexual differentiation milestones (in other words, a full assessment of preputial separation, vaginal patency and nipple retention) and sperm measurements (in other words sperm count, motility and morphology) was lacking. Given the endocrine-active nature of iprodione, as outlined above, there remains uncertainty as to the implication on the development of the young.

With respect to potential pre-natal toxicity, there was no evidence of fetal sensitivity in the rabbit developmental toxicity studies. In the rabbit, abortions and fetal skeletal anomalies were observed only at high doses that also caused significant maternal toxicity. In one rat developmental toxicity study, smaller fetuses were noted at non-maternally toxic doses. In a more recent study, decreased anogenital distance indicative of altered fetal androgen levels was noted at a maternally toxic dose. The finding was supported by a post-natal study in rats from the scientific literature showing a delay in preputial separation at similar dose levels. In the acceptable reproductive toxicity study in the rat, reduced live births, litter size and pup viability were noted at maternally toxic doses.

Neurotoxic effects occurred at dose levels higher those resulting in endocrine-mediated toxicity and likely represented a secondary response to treatment.

For acute risk assessments, the decreased anogenital distance was considered a serious endpoint but was tempered by the presence of maternal toxicity. In consideration of this, the *Pest Control Products Act* factor was reduced to 3-fold when this endpoint was selected for risk assessment. For risk assessments involving repeat-exposure, a 3-fold *Pest Control Products Act* factor was selected to address data uncertainties relating to sensitivity of the young and accommodates other uncertainties in the database (for example, the point of departure for testosterone).

3.2 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to iprodione from potentially treated imported foods is also included in the assessment. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when dietary exposure exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessment procedures.

Residue estimates used in the dietary risk assessment (DRA) may be based conservatively (in other words, upper bound estimates) on the maximum residue limits (MRL) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP). Specific and empirical processing factors, as well as specific information regarding percent of crops treated may also be incorporated to the greatest extent possible.

In situations where the need to mitigate dietary exposure has been identified, the following options are considered. Dietary exposure from Canadian agricultural uses can be mitigated through changes in the use pattern. Revisions of the use pattern may include such actions as reducing the application rate or the number of seasonal applications, establishing longer pre-harvest intervals (PHIs), and/or removing uses from the label. In order to quantify the impact of such measures, new residue chemistry studies that reflect the revised use pattern would be required. These data would also be required in order to amend MRLs to the appropriate level. Imported commodities that have been treated also contribute to the dietary exposure and are routinely considered in the risk assessment. The mitigation of dietary exposure that may arise from treated imports is generally achieved through the amendment or specification of MRLs.

Acute, chronic and cancer dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998. For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendices IV and V, respectively.

For iprodione, residues estimates were primarily based on surveillance data. When surveillance data were not available for a crop, the residue estimate was based on the MRL or the American tolerance level. Percent crop treated data, food supply information, and chemical specific processing factors were incorporated into the estimates where available. Overall, the residue estimates and the dietary exposure assessments are considered to be refined.

3.2.1 Determination of Acute Reference Dose

Females 13-49 years of age

To estimate dietary risk from a single exposure, an oral developmental toxicity study in the rat was selected. The critical effect is a biologically significant decrease in anogenital distance in male rat fetuses at 120 mg/kg bw/day; the NOAEL was 20 mg/kg bw/day. This decrease occurred in the presence of maternal toxicity. Standard uncertainty factors of 10-fold for inter-species extrapolation and 10-fold for intra-species variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 3-fold, yielding a composite assessment factor (CAF) of 300.

The ARfD is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{20 \text{ mg/kg bw}}{300} = 0.067 \text{ mg/kg bw of iprodione}$$

General population (excluding females 13-49 years of age):
With respect to all other populations, there was no endpoint identified in the database considered relevant for the establishment of an ARfD.

3.2.2 Acute Dietary Exposure and Risk Assessment (Food Only)

Acute dietary risk is calculated considering the highest ingestion of iprodione residues that would be likely on any one day from food commodities. A probablistic analysis allows all possible combinations of consumption and residue levels to estimate a distribution of the amount of iprodione residue that might be consumed in a day. A value representing the high end (99.9th percentile) of this distribution is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered not of concern.

The acute exposure at the 99.9th percentile accounted for less than 11% of the ARfD for females 13-49 year old and is, therefore, not of concern. As indicated in section 3.2.1, only the female 13-49 year old population was assessed for acute exposure and risk, as there were no acute toxicological effects identified for other population groups.

3.2.3 Determination of Acceptable Daily Intake (ADI)

To estimate risk from repeated dietary exposure, a 1-year dietary study in dogs was selected for risk assessment. The critical effects were endocrine-mediated responses, namely increased adrenal weights and decreases in prostate weights at the lowest dose tested of 4.1 mg/kg bw/day. A NOAEL was not established. The minimal change in prostate and adrenal weight changes as well as the lack of histological correlates at 4.1 mg/kg bw/day suggested that this dose level was approaching a NOAEL. For this reason, an uncertainty factor for use of a NOAEL was deemed unnecessary. Standard uncertainty factors of 10-fold for inter-species extrapolation and 10-fold for intra-species variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 3-fold, yielding a composite assessment factor (CAF) of 300.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{LOAEL}}{\text{CAF}} = \frac{4.1 \text{ mg/kg bw/day}}{300} = 0.014 \text{ mg/kg bw/day of iprodione}$$

The ADI provides a margin of 5100 to the NOAEL for reduced live births, litter size and pup viability, and a margin of 1400 to the NOAEL for decreased in anogenital distance. The ADI is considered to be protective of all populations, including infants and children.

3.2.4 Chronic Dietary Exposure and Risk Assessment (Food Only)

The chronic dietary exposure was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is not of concern.

The chronic potential daily intake accounted for less than 4% of the ADI for all population groups and is, therefore, not of concern.

3.2.5 Cancer Potency Factor

An increase in four tumour types was noted in the iprodione database, namely liver and ovarian tumors in mice and testicular and uterine tumours in rats. With respect to the Leydig cell tumours in the chronic/carcinogenicity study in rats, characterization of the risk using a threshold mode-of-action has been undertaken at this time despite some uncertainty regarding the point of departure. Use of the LOAEL of 4.1 mg/kg bw/day from the one-year dog study and a CAF (or margin of exposure [MOE]) of 300 for intermediate and long-term risk assessment provides a margin in excess of 400 to the dose at which low level precursor changes were detected; this margin is considered adequate.

A linear low dose extrapolation could not be undertaken for the uterine adenocarcinomas noted in one of the rat studies due to lack of histopathology of the uterus in all animals in the low and mid- dose groups. A linear low dose extrapolation was conducted on the remaining tumour types and of those, the combined incidence of hepatocellular adenomas and carcinomas in male mice yielded the most potent unit risk (q_1*) of 8.89×10^{-3} (mg/kg bw/day)$^{-1}$.

For 3,5-dichloroaniline, a metabolite of iprodione, the q_1* is based on tumours observed with chronic dietary exposure to a structural analog, p-chloroaniline. The q_1* is 6.38×10^{-2} (mg/kg bw/day)$^{-1}$ based on an increased incidence of hemangiosarcomas (spleen) in rats.

3.2.6 Cancer Dietary Exposure and Risk Assessment (Food Only)

The lifetime dietary exposure for iprodione was calculated by using the average consumption of different foods and the average residue values on those foods for the general population (in other words, similar to the chronic intake). The expected intake of residues is then multiplied to the q_1* to determine the lifetime cancer risk. A lifetime cancer risk that is less than one-in-a-million (1×10^{-6}) is considered not of concern for the general population when exposure occurs through pesticide residues in/on food and drinking water, and to otherwise unintentionally exposed persons.

Based on the q_1* approach, the lifetime cancer risk for iprodione was determined to be 1×10^{-6} for the general population and is not of concern. However, the cancer risk from food alone reached the benchmark of 1×10^{-6}. As such, critical commodity analysis of the assessment was conducted to determine the major exposure and risk contributors.

The critical commodity analysis indicated that the major exposure and risk contributors are from peaches, nectarines, and other stone fruits. The residue estimates for stone fruits were based on CFIA monitoring data, which analyzed samples from both domestic production and imported sources. There were relatively high residues found in stone fruits imported from South America as compared to all other foods.

There were adequate data to indicate that 3,5-DCA is not formed in significant amounts in food commodities as a result of iprodione use. Thus, there are no risk concerns from potential 3,5-DCA exposure in food sources.

3.3 Exposure from Food and Drinking Water

3.3.1 Concentrations in Drinking Water

3.3.1.1 Water Modelling

Iprodione and its transformation product RP30228 were modelled in potential groundwater and surface water sources. The initial modeled estimated environmental concentrations (EECs) in groundwater were much higher than surface water EECs, as such groundwater EECs were chosen for use in the dietary exposure and risk assessment. Level 2 groundwater EECs were calculated using the leaching estimation and chemistry model (LEACHM).

When groundwater modelling for iprodione and RP30228 was conducted initially, two separate sets of EECs for RP30228 were generated, based on different estimates of the rate of transformation (in soil) from iprodione to RP30228. These were termed "slow soil rate" and "fast soil rate." Both transformation rates were faster than those measured in the laboratory, because they incorporated hydrolysis as an additional transformation process, but the "fast soil rate" incorporated faster transformation in the topsoil, which, in the LEACHM model allowed for additional degradation of RP30228, and resulted in lower EECs for RP30228. For this reason only the EECs from the "slow soil rate" transformation rate was used, which can be considered conservative estimate of RP30228 concentrations in groundwater.

The overestimation of the transformation of iprodione to RP30228 also means that the EECs for iprodione shown in Appendix VIII – Table 18, which are from a model run considering only iprodione, and used faster transformation rates than the model run used for RP30228, are likely too low. For this reason the EECs for iprodione should not be considered to be conservative estimates.

For the water modelling, three use patterns were modeled, representing use on turf, orchard and canola. For each use pattern, two to four initial application dates were run with LEACHM with applications in all 50 years of the model run. The typical yearly application rate of iprodione for turf use at 8640 g a.i./ha was used, split between three applications: one application of 5760 g a.i./ha in late fall and two applications of 1440 g a.i./ha in the spring. Lower application rates are used for orchard and canola: 750 g a.i./ha and 374 g a.i./ha applied once per year, respectively. The modelled daily and yearly 90th percentile groundwater EECs for iprodione and RP30228 for the application date producing the largest EECs, as well as the 50-year averaged EECs are listed in Appendix VIII – Table 18. The daily 90th percentile, yearly 90th percentile and 50 year average EECs for RP30228 were used for the acute, chronic and cancer dietary exposure and risk.

assessments, respectively. The EECs for iprodione were much lower than the EECs for RP30228 and were not included in the assessments.

Uncertainties and caveats
While more realistic than a model in which iprodione and RP30228 are considered to be a single chemical, the LEACHM model can still not simulate all natural processes. For example, the model transforms the iprodione directly into RP30228 which is contrary to the submitted degradation pathway in which there is an intermediate transformation product.

- The degradation rate of RP30228 was based on data showing the formation and decline of RP30228 in a study measuring the degradation of iprodione. As such, there is more uncertainty in this value than a study intended to measure degradation of RP30228.
- Hydrolysis of iprodione to RP30228 in pH 7 buffer is much faster than transformation of iprodione in soil, which should include any hydrolysis as part of the overall transformation in soil. These two processes were added together in modelling, resulting in a likely overestimate of the conversion rate from iprodione to RP30228. For this reason, the iprodione EECs listed in Appendix VIII – Table 18 should not be considered conservative estimates, but the EECs of RP30228 can be considered as conservative estimates.

Additional information on water modelling:
- Confidence in the modelling results could be improved by determination of an iprodione field degradation rate determined by some means that could identify a suitable mass balance. Further confirmation or validation of transformation chemistry and fate data would also improve confidence in results.
- There is insufficient data to model the transformation product 3,5-DCA.
- Additional use information such as lower rates, fewer applications or years without use could lower predicted EECs.

3.3.1.2 Water Monitoring

Limited surface water and groundwater monitoring data were available in the United States and Canada for iprodione. For the transformation products, isoiprodione (RP30228) and 3,5-DCA, limited data were available in the United States, however, no monitoring data for the transformation products were available in Canada. Overall, the monitoring data indicate that iprodione and isoiprodione can reach groundwater, however, measured concentrations in high use areas were less than 1 µg/L and detections were sporadic. The monitoring data do not provide an adequate basis to confirm the significance of this exposure route in risk assessment because of the associated uncertainties with the available data.

Groundwater
Only one study conducted in California in 1998 monitored the residues of iprodione and RP30228 in groundwater. In that study, iprodione was not detected and RP30228 was detected below the LOQ <0.025 µg/L in only one sample out of 239 water samples analyzed. The rest of the studies including the registrant sponsored study conducted in Suffolk County, New York, monitored either only iprodione or iprodione and 3,5-DCA (a product identified to be of health concerns to United States Environmental Protection Agency [USEPA]). There was no detection

of iprodione. The sparseness of monitoring data deterred the determination of EECs for use in human health exposure assessment.

Surface water
Similar to groundwater, only one study monitored the residues of iprodione and RP30228 in surface water. This study, sponsored by the registrant, was conducted in Florida, New Jersey and Illinois regions. These sites were selected because their source water (Community Water Systems) originates from water sheds in high iprodione use and sales areas. Raw and finished water samples were sampled over a period of three years. Detections of iprodione and RP30228 were observed only in the sites from New Jersey. At the New Jersey site, out of 109 raw samples, iprodione was detected 31 times in three years; twenty two times were above the LOQ with a peak concentration of 0.559 µg/L. RP30228 was detected 19 times in three years with 10 detections above the LOQ and a peak concentration of 0.309 µg/L. 3,5-DCA was not detected above the LOQ in raw water samples in three years; only one detection occurred with a concentration less than the LOQ.

Iprodione was detected ten times in 105 finished water samples in the three years with four detections above the LOQ ranging from 0.062 to 0.221 µg/L. Iprodione and RP30228 were detected at less than the LOQ, six and four times, respectively, in the three years. No 3,5- DCA was detected in finished water. This study indicates that the occurrence of iprodione -related residues are sporadic and very low in concentration (less than 1 µg/L).

3.3.2 Dietary Food and Drinking Water Exposure and Risk Assessment

As indicated in section 3.3.1.1, food and drinking water exposure and risk estimates were determined using multiple EECs. The EECs were based on modelling of iprodione and metabolite residues in groundwater using either the typical use rates for turf, orchard, or canola applications.

When using EECs based on the turf application rate, the acute exposure from food and drinking water accounted for less than 53% of the ARfD for the female 13-49 year old population group. An acute dietary risk assessment was not required for any other population groups. The chronic exposure accounted for less than 60% of the ADI for all population groups except infants (<1 years old), where the exposure accounted for 126% of the ADI. The cancer risk was determined to be 8 × 10^{-7} for the general population.

When using EECs based on the orchard application rate, the acute exposure from food and drinking water accounted for less than 12 % of the ARfD for the female 13-49 year old population group. The chronic exposure accounted for less than 15% of the ADI for all population groups. The cancer risk was determined to be 5 × 10^{-8} for the general population.

When using EECs based on the canola application rate, the acute exposure from food and drinking water accounted for less than 12% of the ARfD for the female 13-49 year old population group. The chronic exposure accounted for less than 9% of the ADI for all population groups. The cancer risk was determined to be 3 × 10^{-8} for the general population.

In summary, the estimated acute and chronic exposures from iprodione in food and drinking water were below the ARfD and ADI for most of the population groups and use rates assessed. However, the cancer risk exceeded 1×10^{-6} for the general population for all use rates assessed and is of concern. The cancer risk estimates ranged from 5×10^{-5} to 8×10^{-5}. Exposure from drinking water was the major risk contributor in the assessment for all use scenarios. As indicated in Section 3.2.6, the exposure from food commodities alone was also a significant contributor in the cancer assessment with an estimated risk of 1×10^{-5}.

3,5-Dichloroaniline (DCA)
3,5-DCA is a terminal metabolite of iprodione that can potentially be formed in water. As indicated in section 3.2.5, this metabolite may be carcinogenic and has an estimated q_1^* of 6.39×10^{-2} (mg/kg bw/day)$^{-1}$.

There are currently insufficient data available to the PMRA to adequately estimate 3,5-DCA concentrations in drinking water. As such, a quantitative exposure and risk assessment for 3,5-DCA could not be conducted. This is a major gap in the overall risk assessment.

The PMRA will not require additional data for 3,5-DCA at this time given the risk concerns identified from iprodione and other metabolites. However, additional data related to 3,5-DCA would be required for continued registration if interested parties wish to submit a data package to further refine the current dietary assessment and address the risk concerns identified.

It should be noted that the data gaps for 3,5-DCA are related to drinking water only.

3.6 Occupational and Non-Occupational Exposure and Risk Assessment

The occupational and non-occupational non-cancer risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive sub-population. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

The cancer risk is determined by calculating the lifetime average daily dose (LADD) from dermal and inhalation exposure. The LADD is multiplied by the q_1^* to obtain a lifetime cancer risk estimate, which is the measurement of probability. A lifetime cancer risk in the range of 1 in 10^{5} in worker populations and in the range of 1 in 10^{6} in residential populations is generally considered acceptable.

3.6.1 Toxicology Endpoint Selection for Occupational and Non-Occupational Risk Assessment

For short-term dermal and inhalation:
The 15-wk dietary toxicity study in rats was selected for use in risk assessment, as the existing repeat dose dermal toxicity study did not include microscopic examinations of target organs and no suitable repeat-dose inhalation toxicity study was available. The critical effects were decreases in testes and prostate weights, as well as increases in adrenal weights at 51 mg/kg bw/day; the NOAEL was 17 mg/kg bw/day. For occupational exposure, the MOE is 300, which

includes standard uncertainty factors of 10-fold for inter-species extrapolation and 10-fold for intra-species variability. As the worker population could include pregnant and/or nursing women, it is necessary to afford adequate protection of the fetus or infant who may be exposed via its mother. An additional 3-fold factor accounts for the uncertainty in relation to potential effects on the onset of puberty and sexual differentiation that could result from in utero or lactational exposure.

For non-occupational exposure, the target MOE is 300 which includes standard uncertainty factors of 10-fold for inter-species extrapolation, 10-fold for intra-species variability and the 3-fold *Pest Control Products Act* factor based on the rationale provided in the *Pest Control Products Act* Hazard Consideration section.

For intermediate-/long-term dermal and inhalation:
A 1-year study in dogs was selected for use in risk assessment as the existing repeat-dose dermal toxicity study did not include microscopic examinations of target organs and no suitable repeat-dose inhalation toxicity study was available. The critical effects were endocrine-mediated responses, namely increased adrenal weights and decreases in prostate weights at the lowest dose tested, 4.1 mg/kg bw/day. A NOAEL was not established. The minimal change in prostate and adrenal weight as well as the lack of histological correlates at 4.1 mg/kg bw/day, suggested that this dose level was approaching a NOAEL. For this reason, an uncertainty factor for use of a LOAEL was deemed unnecessary. A target MOE of 300 was established which included standard uncertainty factors of 10-fold for inter-species extrapolation, 10-fold for intra-species variability and an additional 3-fold factor. This latter factor accounts for the uncertainty in relation to potential effects on the onset of puberty and sexual differentiation that could result from in utero or early life exposure.

Cancer
As noted in Section 3.2.5, a q_1^* of 8.89×10^{-3} (mg/kg bw/day)$^{-1}$ has been determined for iprodione.

3.4.2 Dermal Absorption

The estimated dermal absorption is based on an in vivo rat dermal absorption study. A dermal absorption value of 16% was used in estimating the systemic dose from dermal exposure for the cancer and non-cancer risk assessment.

3.4.3 Occupational Exposure and Risk Assessment

Workers can be exposed to iprodione through mixing, loading or applying the products containing the pesticide, and when entering a treated site to conduct activities such as scouting and handling treated crops or seeds.

3.4.3.1 Mixer, Loader and Applicator Exposure and Risk Assessment

The following exposure scenarios were considered:

- Mixing/loading of wettable (soluble) powder;
- Mixing/loading of suspension;

- Mixing/loading of wettable granules;
- Mixing/loading of granules;
- Airblast liquid application to fruit trees, grapes, raspberries, cauliflower, cabbage, conifer seedlings, and ornamentals;
- Groundboom liquid application to turf, berries, lettuce, cauliflower, cabbage, snap beans, ginseng, dry common beans, canola, alfalfa (for seed), conifer seedlings, and ornamentals;
- Aerial liquid application to snap beans, dry common beans, and canola;
- Granular application to turf;
- Manually pressurized handwand liquid applications to fruit trees, grapes, berries, ginseng, greenhouse vegetables, conifer seedlings, and ornamentals;
- Mechanically pressurized handgun liquid applications to fruit trees, grapes, greenhouse vegetables, conifer seedlings, and ornamentals;
- Backpack liquid application to turf, fruit trees, grapes, berries, ginseng, greenhouse vegetables, conifer seedlings, and ornamentals;
- Handheld and stationary mist blower application in greenhouses;
- Handheld and stationary fogger application in greenhouses;
- Commercial mixing, loading, and applying liquid treatments to canola and mustard seed;
- On-farm mixing, loading, and applying liquid seed treatment to canola and mustard seed;
- Commercial and on-farm mixing, loading, and applying liquid potato seed piece treatment and planting treated potato seed;
- Planting of commercially treated canola, mustard, and carrot seed;
- Garlic dip.

Based on the number of applications and timing of application, workers applying iprodione would generally have a short-term (<30 days) duration of exposure. Custom applicators may have longer (for example, up to several months) exposure for crops with multiple applications; however, the short-term toxicological endpoint is based on a 13-week study and is therefore applicable for this duration. An exception would be for greenhouse crops, which are considered to have intermediate- to long-term (for example, greater than several months) duration of exposure.

The PMRA estimated handler exposure is based on different levels of personal protective equipment (PPE) and engineering controls.

- Baseline PPE: Long pants, long-sleeved shirt and chemical-resistant gloves (unless specified otherwise). For groundboom application, this scenario does not include gloves, as the data quality was better for non-gloved scenarios than gloved scenarios.
- Mid-Level PPE: Cotton coveralls over long pants, long-sleeved shirt and chemical-resistant gloves.
- Maximum PPE: Chemical-resistant coveralls over long-sleeved shirt, long pants and chemical-resistant gloves
- Engineering Controls: Represents the use of appropriate engineering controls, such as closed cab tractor or closed loading systems. For groundboom and airblast applicators,

the engineering controls comprised closed cab and baseline PPE. Engineering controls are limited for handheld application methods.

- Headgear [airblast application only]: Open cab, chemical-resistant coveralls over long sleeved shirt, long pants, chemical-resistant headgear that covers the neck (for example, Sou'Wester hat, rain hat) and chemical-resistant gloves.
- Respirator: a NIOSH-approved respirator with a canister approved for pesticides.

No appropriate chemical-specific handler exposure data were available for iprodione; therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED) Version 1.1, and the Agricultural Handler Exposure Task Force (AHETF).

The PHED is a compilation of generic mixer/loader/applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment (PPE). In most cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing coveralls, chemical-resistant coveralls or a respirator. This was estimated by incorporating a 75% clothing protection factor for coveralls, a 90% clothing protection factor for chemical-resistant coveralls, and a 90% protection factor for a respirator into the unit exposure values. Inhalation exposures were based on light inhalation rates (17 L/min) except for backpack applicator scenarios, which were based on moderate inhalation rates (27 L/min).

The unit exposures for the open cab airblast scenario were available from the AHETF database. Inhalation unit exposures are based on light inhalation rates (17 L/min) unless otherwise stated.

Iprodione is registered for seed and potato seed piece treatments. PHED scenarios were not considered to be representative of exposure to workers treating or handling seed or seed pieces. Surrogate commercial and on-farm seed treatment exposure studies, as well as exposure studies for planting treated seeds, were used to estimate worker exposure.

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The generation of exposure data representative of modern application equipment and engineering controls may potentially refine the risk assessment. Biological monitoring data could also further refine the assessment.

Occupational non-cancer risk estimates associated with mixing, loading, and applying iprodione are summarized in Appendix VI. For short-term exposure durations, the same toxicological endpoint and target MOE was applicable to for both dermal and inhalation exposure routes. Thus, it is appropriate to combine the route-specific MOEs to generate a single risk estimate. The dermal and inhalation exposure was combined and risk was calculated using the oral toxicological study, as per the following equation:

$$\textbf{Combined MOE} = \frac{\textbf{Oral NOAEL}}{\textbf{Dermal Exposure} + \textbf{Inhalation Exposure}}$$

Occupational cancer risk estimates associated with mixing, loading, and applying iprodione are summarized in Appendix VI. The LADD is calculated assuming 40 years of exposure (in other words, a career in agriculture of 40 years) over a 78-year lifetime. Farmer applicators were considered to be exposed up to 30 days per year and custom applicators were assumed to be exposed for 30 days per year based on the number of applications per year.

For most formulations, based on the current label PPE and application rates, there are some calculated MOEs that are below the target MOE, and are of concern.

For most formulations, based on the current label PPE and application rates, there are some calculated cancer risk estimates that are above 1×10^{-5} and are of concern.

Data were not available to assess worker exposure from handheld mist blowers and foggers in greenhouses. Exposure is expected to be significant, especially due to potential inhalation of mist and/or fog. Data or label restrictions would be required for this use.

For commercial garlic seed treatment and planting of treated garlic seeds, adequate data to estimate exposure were not available. Data would be required for this use.

3.4.3.2 Post-application Worker Exposure and Risk Assessment

The post-application occupational risk assessment considers exposures to workers who enter treated sites to conduct agronomic activities involving foliar contact (for example, pruning, thinning, harvesting or scouting). Based on the iprodione use pattern, there is potential for short- to intermediate-term (>1 day to several weeks) post-application exposure for most scenarios. For greenhouse uses, there is potential for intermediate- to long-term (from several months to a year) post-application exposure.

Potential exposure to post-application workers was estimated using updated activity-specific transfer coefficients (TCs) and dislodgeable foliar residue (DFR) or turf transferrable residue (TTR) values. The DFR or TTR refers to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant. The TC is a measure of the relationship between exposure and DFRs for individuals engaged in a specific activity, and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Activity-specific TCs from the Agricultural Re-Entry Task Force (ARTF) were used. Post-application exposure activities for agricultural crops include (but are not limited to): harvesting, pruning, scouting and thinning.

Chemical-specific DFR and TTR studies available in the literature and submitted to the PMRA were considered in the post-application risk assessment. Of these, four studies were considered acceptable for risk assessment purposes. The amount of dislodgeable residue is expected to be the same for each formulation. Most formulations are designed to dissolve in water before application. The study and site selected to estimate DFR on registered Canadian crops were calculated, where possible, using the study peak DFR and predicted percent dissipation per day calculated from the linear equation of plotting the natural logarithm of DFR versus dissipation time (post-application interval) following the final application. Although these studies reflected the current use pattern of iprodione, the study design precluded estimating exposure when possible mitigation measures are considered (in other words, reduced number of applications and increased application intervals). Estimated DFR values were adjusted proportionally for maximum Canadian application rates. There were no DFR studies available for greenhouses; therefore the default peak residue of 25% was used; however, as the dissipation rate inside greenhouses is unknown, the dissipation of residues over time could not be estimated.

Due to the limited number of acceptable DFR studies available to the PMRA for the post-application risk assessment, the extrapolation of study DFR data to a wide variety of crops was required. Extrapolation was based on a comparison of general crop morphology, application equipment, application regime, foliage types, application rates, study conditions and climatic zones. Since the studies available are not necessarily representative of some Canadian crops, this extrapolation represents an uncertainty in the post-application assessment.

For workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required before workers can enter after application to perform tasks involving hand labour. An REI is the duration of time that must elapse in order to allow residues to decline to a level where there are no risks of concern for post-application worker activities (for example in the case of iprodione, performance of a specific activity that results in exposures above the target MOE of 300 for dermal exposure, or below the cancer threshold of 1×10^{-5}).

Based on current label rates, in order to achieve the target MOE or the cancer threshold for post-application workers in agricultural scenarios, most current REIs would need to be increased in duration. Calculated REIs ranged from 12 hours to 137 days for outdoor uses. For most greenhouse uses, REIs cannot be determined. Appendix VI summarizes the post-application exposure risk assessment.

Some proposed REIs may be considered agronomically feasible for crops; however some may not be feasible, especially those for: greenhouse cut flowers, greenhouse tomatoes, greenhouse cucumbers, grapes, cauliflower, cabbage, outdoor cut flowers, cherries, peaches, plums, prunes, apricots, leek, onion, raspberries, and some outdoor ornamentals.

3.4.4 Non-Occupational Exposure and Risk Assessment

Non-occupational or residential risk assessment involves estimating risks to the general population, including children and youths, during or after pesticide application. There are no registered domestic class products for iprodione; however, there is potential for exposure during golfing on treated turf, or through bystander exposure.

The USEPA has generated standard default assumptions for developing residential exposure assessments for both applicator and post application exposures when chemical- and/or site-specific field data are limited. These assumptions may be used in the absence of, or as a supplement to, chemical- and/or site-specific data and generally result in high-end estimates of exposure. These assumptions are outlined in the Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessments (2012). The following sections from the Residential SOPs were used to assess residential exposure to iprodione:

- Section 3: Lawns and Turf (golfing)
- Section 7: Indoor Environments

Many chemical-specific studies were found in the literature measuring iprodione in house dust, floors, clothing, toys, indoor and outdoor air. Of these, only point estimates were used to create a high end estimate of potential exposure.

Residential Handler Exposure and Risk Assessment

As no domestic class products are registered for iprodione, a residential handler assessment was not required.

Residential Post-application Exposure and Risk Assessment

There is potential for residential exposure to iprodione applied in agricultural areas due to the proximity of homes in agricultural areas or through spray drift. There is potential for non-dietary incidental exposure for children. Residues of iprodione were measured in dust, floors and ambient air as reported in the literature.

The following scenarios were assessed for residential exposure to iprodione:

- dermal exposure during golfing for adult, youth and children (6 to <11 years old)
- hand-to-mouth exposure to dust on floors for children (1<2 years old)
- ingestion of dust in homes for children (1<2 years old)
- inhalation of ambient air for adult, youth and children

Quantitative estimates of exposure and risk were determined for iprodione, based on the available data or using standard defaults in the absence of data. Estimates of exposure did not reach the target MOE or cancer threshold for adults and children for all scenarios, and are, therefore, not of concern.

3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, as well as from all known or plausible exposure routes (oral, dermal and inhalation).

3.5.1 Toxicology Endpoint Selection for Aggregate Risk Assessment

Aggregate Short Term (all populations)
The 13-week dietary toxicity study in the rat was selected for use in risk assessment as the existing repeat-dose dermal toxicity study did not consider target organ information and no suitable repeat-dose inhalation study was available. The critical effects were decreases in testes and prostate weights, as well as increases in adrenal weights at 31 mg/kg bw/day; the NOAEL was 15 mg/kg bw/day. A target MOE of 300 was established which included standard uncertainty factors of 10-fold for inter-species extrapolation and 10-fold for intra-species variability as well as a 3-fold *Pest Control Products Act* factor. This latter factor accounts for the uncertainty in relation to the onset of puberty and sexual differentiation that could result from in utero or early life exposure.

3.5.2 Residential and Non-occupational Aggregate Exposure and Risk Assessment

An aggregate assessment (non-cancer and cancer) for iprodione was not conducted as risk concerns were already identified from food and drinking water.

3.6 Cumulative Risk Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current re-evaluation, the PMRA did not identify information indicating that iprodione shares a common mechanism of toxicity with other pest control products. Therefore, there is no requirement for a cumulative assessment at this time.

3.7 Incident Reports Related to Human Health

Since 26 April 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects to Canadian health or the environment. Incident reports involving the active ingredient iprodione were reviewed.

As of 24 March 2015, the PMRA had received two human and one domestic animal incident report.

All symptoms were classified as either minor or moderate in severity and were determined to have some degree of association with the stated exposure scenario. Each exposure scenario was different, and there were no commonalities in symptoms reported.

No label changes resulting from these incident reports are considered necessary at this time.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Terrestrial and aquatic environmental fate data for iprodione is summarized in Appendix VIII, Table 1. A list of major transformation products (chemical name, code number and structure) is provided in Appendix VIII, Table 2; in the text of this document, transformation products are referred to by their code number.

Based on its physical properties, iprodione is soluble in water and has a low potential to volatilize from moist soil or water surfaces (vapour pressure = 2.7×10^{-7} mm Hg, Henry's Law constant = 1.2×10^{-7} atm.m^3/mol). Hydrolysis is not an important route of transformation of iprodione under acidic conditions. However, hydrolysis of iprodione is shown to increase with increasing pH; (in other words, the hydrolysis half-life for iprodione at pH 7 and 9 at 25°C is 6.4 days and 27 minutes, respectively). Therefore hydrolysis of iprodione may be an important route of transformation under neutral and alkaline conditions. RP35606 and RP30228 are identified as major hydrolysis products. Iprodione is shown to photolyze in soil with DT_{50}s ranging from 7 – 14 days. The major phototransformation product identified in soil was RP32596. Photolysis of iprodione in soil is not considered to be an important route of transformation.

The log octanol/water partitioning coefficient for iprodione (Kow = 3.1) suggests the potential for bioaccumulation in the food chain. Based on bioconcentation data for freshwater fish (bioconcentration factor of 72 and depuration time < 1 day in bluegill sunfish), the potential for bioaccumulation is expected to be low.

Iprodione enters the terrestrial environment when it is used as a fungicide on a variety of crops, outdoor ornamentals, forest and woodlots, golf course turf, and as a seed treatment. In the terresterial environment, iprodione is expected to be slightly to moderately persistent under aerobic conditions depending on the soil type (DT_{50} = 16–172 days). The major transformation products identified under aerobic laboratory conditions are RP30228 and RP36221. Under anaerobic soil conditions, iprodione biotransforms more readily and is considered slightly persistent (DT_{50} = 21–26 days); only one major transformation product, RP30228, was identified under anaerobic soil conditions. Adsorption data indicate that iprodione has low to medium mobility in soils.The organic matter content appears to be the primary factor affecting the mobility of iprodione in soils; mobility decreases as the organic matter content of the soil or sediment increases. The transformation product RP32596 is shown to have low mobility in soil and RP30228 is immobile. Soil column leaching experiments reveal that most of the applied iprodione remains in the top 20 inches of soil except in sand soil (that is low in organic matter) where considerable leaching may be expected. The leaching assessment using the groundwater ubiquity score (GUS[5]) indicates that iprodione is a leacher under some soil conditions and satisfies most of the criteria of Cohen *et al.* 1984[6]. Groundwater modelling, which utilized a scenario that would result in the conservative estimation of leaching, also indicates that iprodione may reach groundwater. Terrestrial field studies from a Canadian or American equivalent ecoregion were not available. However, based on studies conducted in California, North Carolina and various sites in Western Europe, iprodione residues were not detected beyond the 10–30 cm soil depth. As these studies were conducted in silt loam, loamy sand or sandy loam soil, it does not preclude the potential leaching of iprodione to grourdwater when it is applied to sand soil. Canadian groundwater monitoring data, although limited, shows no detection of iprodione in groundwater samples.

Iprodione can enter aquatic environments through spray drift and run-off from the application site. Phototransformation is not expected to contribute to the dissipation of iprodione from the water layer in the photic zone. In aquatic environments, iprodione is expected to be non-persistent under aerobic and anaerobic conditions. As the aerobic aquatic biotranformation laboratory studies were conducted using alkaline waters, conditions in which iprodione hydrolyses rapidly, hydrolysis may have played a major role in the transformation of iprodione 1979conditions. The major transformation products identified under aerobic aquatic conditions were RP30228 and RP32490; RP30228 partitions mainly into the sediment phase whereas RP32490 predominantly remains in the water phase. RP30228 was the only major transformation product identified under anaerobic aquatic conditions.

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[5] Gustafson, D.I. 1989. Groundwater ubiquity score: a simple method for assessing pesticide leachability. Environmental Toxicology and Chemistry, 8: 339–357. (PMRA 1918524).

[6] Cohen, S.Z., Creeger, S.M., Carsel, R.F., Enfield, C.G. 1984. Potential for pesticide contamination of groundwater resulting from agricultural uses. (PMRA 1573066).

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted using uncertainty factors to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints.

Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

A summary of terrestrial toxicity data for iprodione is presented in Appendix VIII, Table 3; some toxicity data on the transformation products (RP30228 and RP32596) were also available. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with iprodione. The terrestrial assessment took into account the range of agricultural application rates that are registered for iprodione, taking into consideration that there may be multiple applications of iprodione in a use season.

Terrestrial Invertebrates
Earthworms
The most sensitive LD_{50} for soil dwelling organisms exposed to iprodione is > 100 mg a.i./kg soil for springtails (*Folsomia candida*). At the highest cumulative application rate (9000 g a.i./ha

× 3 applications @ 14 d for turf use), the calculated EEC in soil is 10.7 mg ai/kg soil. The RQ indicates that the LOC for acute effects is not exceeded for soil dwelling organisms (RQ < 0.1).

Chronic earthworm toxicity study for iprodione, RP30228 and 3,5-DCA were available for review; the 8-week NOEC for *Eisenia andrei* exposed to iprodione and RP30228 was 1000 mg a.i./kg soil and 100 mg a.i./kg soil for *Eisenia fetida* exposed to 3,5-DCA. At the highest cumulative application rate (9000 g a.i./ha for turf use), the calculated EEC in soil for the transformation products RP30228 and 3,5-DCA is 10.7 and 5.2 mg a.i./kg soil. Risk of chronic effects to earthworms from exposure to iprodione, RP30228 or 3,5-DCA is not anticipated as the risk quotients do not exceed the level of concern (RQ = 0.02 for iprodione and RP30228, and RQ = 0.1 for 3,5-DCA).

Bees

Pollinators can be exposed to iprodione from contact and/or feeding on contaminated parts of plants, for example, pollen and nectar that are sprayed during bloom. In-hive bees, including immature bees, can be exposed via contaminated plant materials brought back by foraging bees. For Tier I risk assessment for foliar application, to be conservative, the highest application rate to flowering crops (cauliflower - 1.5 kg a.i./ha) was used to estimate the environment exposure concentration (EEC).

The tier I risk quotient for acute contact and oral toxicity to honeybee adults does not exceed the level of concern at the highest agricultural crop application rate. No laboratory studies were provided for chronic effects on adult bees. Significant larval bee mortality was observed in a laboratory study designed to examine the dietary effect of iprodione on the growth and development of bee larvae; a suitable endpoint, however, could not be derived from the results (in other words, only a single dietary exposure dose was used) and the environmental relevance of the exposure is uncertain.

In a tier II study, exposure of adult female bees (*Osmia lignaria*) to iprodione applied to lacy scorpionweed, (*Phacelia tanacetifolia*) at 1.12 kg a.i./ha under semi-field conditions (caged bees) did not adversely affect survival, foraging or nesting behaviour. A higher tier risk assessment could not be conducted as data for field (Tier III) studies were unavailable.

No ecological incidents involving bees have been reported in Canada. Two incidents in the U.S, however, report adverse effects to managed bee colonies used for pollination services (in other words, brood losses, adult bee mortality) attributed to application of iprodione to almond and cherry crops.

Based on the weight of evidence, potential risk of iprodione to bees, especially immature bees, cannot be excluded. Consequently, mitigation on the label would reduce the exposure to bees.

Beneficial arthropods

The risk to beneficial arthropods from exposure to direct application of iprodione was determined based on the most sensitive LR_{50} for the predatory mite *Typhlodromus pyri* and the parasitic wasp *Aphidius rhopalosiphi*. The EECs were determined for both on-field and off-field exposure. The application rates chosen to calculate EECs cover the range of application rates for crops that are compatible with IPM programs.

The iprodione EEC values for beneficial predatory and parasitic arthropods were refined to consider foliar interception. The exposure estimates are assuming deposition to a 2-dimensional structure. Therefore, the values can be corrected to take into account the 3-dimensional structure where a certain fraction is intercepted by the crop (for in-field exposure) or the off-field vegetation (for off-field exposure). For the in-field EEC, crop-specific foliar interception factors are applied to the application rate. For the off-field EEC, a vegetation distribution factor is applied to the application drift rate.

Although the use of iprodione on plums, prunes, and apricots is expected to be compatible with the use of beneficial predatory and parasitic arthropod species in IPM programs, adverse effects could not be ruled out for greenhouse uses or for in-crop arthropod populations at rates used for conifer seedling, outdoor ornamental, cherry, peach, or raspberry crops; risk quotients exceed the LOC for beneficial arthropods for these uses (RQ < 1.3 to 5.5). There is uncertainty associated with the risk calculation which is largely attributed to the lack of a definitive LR_{50} for the indicator species (LR_{50} > 750 g a.i./ha). The available toxicity data were not tested at rates high enough to determine the dose at which 50% mortality occurs. The response at the highest dose tested was 9.0% stimulation of beneficial capacity of *A. rhopalosiphi* and 42% mortality of *T. pyri* in glass plate tests. Therefore, predatory arthropods are more likely to be affected by exposure to iprodione. A precautionary label statement would inform users of the potential risks to beneficial insects. Based on a spray drift assessment, there are no concerns about impacts on beneficial predatory and parasitic arthropod species in habitat adjacent to the treatment area at any of the currently registered rates.

Terrestrial Plants

Suitable data on the toxicity of terrestrial vascular plants for iprodione were not available. According to the 1979 Proceedings of the British Crop Protection Conference Pests and Diseases,[7] iprodione alone or in combination with several other fungicides is not toxic to plants. Given that the mode of action (in other words, inhibition of spore germination and growth of mycelium) does not apply to plants, adverse effects to terrestrial vascular plants are not anticipated. Iprodione is registered for fungicide control on a variety of plant species at a wide range of application rates; no incidents have been reported in Canada that would indicate that iprodione use causes adverse effects to terrestrial vascular plants. In the U.S. damage has been reported to a variety of blueberries (rabbiteye blueberries) after iprodione application (Rovral 4F); the registrant ammended the product label restricting use on rabbiteye blueberries. Iprodione is not registered for use on blueberries; nor is Rovral 4F. Based on the weight of evidence, iprodione is not expected to pose a risk to terrestrial plants.

Terrestrial vertebrates – foliar applications

For the bird and mammal risk assessment, the ingestion of food items contaminated by spray droplets is considered to be the main route of exposure. The risk assessment therefore takes into account the expected concentration of iprodione on various food items immediately after the last application and the food ingestion rate of different sizes of birds and mammals.

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[7] Suta, V., M. Trandafirescu, V. Popescu, E. Voica and S. Fugel. 1979. Proceedings of the British Crop Protection Conference - Pests and Diseases, page 103.

At the screening level, the most conservative exposure estimates are used. For iprodione, the cumulative application rate for turf results in the highest estimated daily exposures (golf course fairways - three applications of 9000 g a.i./ha with a 14 day interval). At this rate, and assuming that birds and mammals were feeding exclusively on one food item with the highest residues, the screening level risk quotients exceed the level of concern for all sizes of birds and mammals both on an acute and reproduction basis. Further characterization of the risk was therefore warranted.

To further characterize the risk to birds and mammals, the assessment was expanded to include a range of iprodione residue concentrations on all relevant food items resulting from the highest application rate for turf use (9000 g a.i. / ha × 3 at 14 d intervals, used at the screening level) but also considering the lowest single and highest cumulative crop application rates (alfalfa – 744 g a.i./ha, and raspberry – 1000 g a.i./ha × 8 at 7-day intervals, respectively)). The risk associated with the consumption of food items contaminated from spray drift off the treated field was also assessed taking into consideration the projected spray deposition at 1 metre downwind from the site of application (6% for ground application to alfalfa and turf with a spray quality of ASAE medium and 74% for airblast application to raspberry with spray quality of ASAE fine). Risk quotients for birds and mammals are shown in Tables 4 and 5 of Appendix VIII, respectively.

For the turf use, given that applications are only made on golf course fairways, short grass was the only food item considered to be relevant for the assessment. Risk quotients calculated using maximum and mean residue concentrations on this food item exceed the level of concern on an acute and reproduction basis for large birds, medium sized mammals and large mammals feeding directly on the treated area. Small and medium sized birds as well as small mammals were excluded from the calculations, as these are not expected to forage exclusively on plant material.

The risk assessment for turf use was based on the highest curative application rate (9000 g a.i./ha) for the control of snow mould; as the maximum number of applications per season for the control of snow mould is not clearly stated on product labels, three applications was chosen based on the maximum seasonal application rate per year supported by the registrant for all turf diseases listed on product labels (27000 g a.i./ha). According to information provided on some product labels and general turfgrass management recommendations (for example, OMAFRA Publication 384, 2005), application of iprodione for the control of snow mould is made in late fall or early winter just prior to ground freezing or before the first snowfall, and may be repeated in mid-winter when turf is free of snow and again immediately after the final snow melt in early spring. In the spring and summer, iprodione can also be applied to turf for the control of other diseases at lower rates ranging from 1500 to 3042 g a.i./ha for preventative application rates and 4576 – 6250 g a.i./ha for curative application rates). Given the range of application rates, and because applications are typically alternated with other fungicides having different mode of action, iprodione is unlikely to be applied three times at the highest curative rate of 9000 g a.i./ha for snow mould control. For this reason, additional turf rates were considered for the assessment. Based on mean residue values, over the preventative and curative rate range for a single application, risk quotients still exceed the LOC for reproductive effects in large birds (RQ = <1.0 – 4.1) and for medium and large sized mammals (RQ = <1.0 – 2.9 and <1.0 – 1.6, respectively) feeding on short grass on turf.

In addition, results of the risk assessment indicate that agricultural uses of iprodione may pose an acute and reproductive risk to birds and reproductive risk to mammals. The risk assessment for agricultural uses was based on the highest cumulative crop application rate and shortest interval (raspberries: 1000 g a.i./ha × 8 applications at 7 day intervals). For the purpose of managing disease resistance to iprodione, all agricultural end-use products labels recommend rotating with fungicides having different mode of action. Furthermore, the typical application rate and number of applications reported by the registrant for iprodione on raspberry is one application per year at 1000 g a.i./ha in British Columbia, Quebec, Ontario, Nova Scotia and Prince Edward Island. British Columbia, Quebec and Ontario are the major raspberry producing provinces. Based on the typical single application rate, the LOC for reproductive effects remain slightly exceeded for small and medium sized birds feeding on insects on-field and adjacent to treated fields (RQ = 2.0 – 2.6 and 1.5 – 1.9, based on mean residue values).

Overall, the risk assessment shows that reproductive effects resulting from turf applications and highest agricultural crop applications of iprodione pose a risk to birds and mammals. Although there are no incident reports involving birds and mammals from the use of iprodione, none would be expected from adverse chronic exposure; chronic problems affecting wildlife from the use of iprodione would be largely unnoticed in the field.

Terrestrial Vertebrates – seed treatments

When pesticides are used as a seed treatment, the treated seed may be consumed as a food item by both birds and mammals. The risk assessment method for treated seed is similar to that of spray applications, except that the dietary items are treated seeds rather than dietary items sprayed with pesticide. Iprodione is registered as a seed treatment for carrot, canola and mustard. A risk assessment was conducted for birds and mammals to address the intake of treated seed.

The exposure of birds and mammals to a pesticide through consumption of treated seed is a function of the amount of pesticide on the seed, the body weight and food ingestion rate of the animal, and the number of seeds available for consumption. In the screening level assessment, it is assumed that the diet consists entirely of treated seeds, and all of the treated seed that is planted is available for consumption *ad libitum*, over an extended period of time. Variables of feeding preference, availability of treated seed, or potential avoidance behaviour toward treated seed are not considered at the screening level.

The risk was assessed using the same generic bird and mammal body weights and toxicity endpoints selected for use in the foliar application risk assessment. To assess the risk to birds and mammals from consumption of treated seeds a risk quotient is calculated by dividing the number of seeds normally consumed per day (Appendix VIII, Table 7) by the number of seeds required to reach the toxicity endpoint (Appendix VIII, Table 6).

The calculated risk quotients are listed in Appendix VIII, Table 8. The calculation of these risk quotients assume that 100% of the seeds consumed by birds and mammals are treated seeds and that all planted seed is available. Risks were found for all birds and mammals.

To further characterize the risk to birds and mammals the assessment was expanded by taking into consideration that not all seeds planted will be exposed and available to birds or mammals. De Snoo and Luttik (2004)[8] reported available seeds of 0.5% for precision drilling, 3.5% for standard drilling in spring, and 9.2% for standard drilling in autumn. This information was used along with typical seeding rate changes for carrot, canola and mustard to estimate the maximum area required for a bird and mammal to find enough seeds to reach the toxicity endpoint; these crops are assumed to be seeded using standard drilling in spring. This refinement does not change the RQ determined, but provides an indication of the area required for a bird and mammal to find enough seeds to reach the toxicity endpoint.

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[8] de Snoo, G.R., R. Luttik (2004) Availability of pesticide-treated seed on arable fields. Pest Management Science 60:501-506.

In most cases, birds and small mammals would need to consume a large number of seeds in order to reach the LOC for acute effects. In addition, as can be noted in Appendix VIII, Table 9, the field area that birds and mammals would have to forage within to find enough seeds to reach the LOC for these effects is relatively large.

For reproductive effects, however, the number of seeds needed to be consumed and the foraging area to reach the LOC is relatively small, particularly for 20 and 100 g birds and 15 and 35 g mammals; the reproductive risk is shown to be much greater for small birds (RQ = 22 – 60) than for small mammals (RQ = 5 – 6). The risks found are only applicable for the few days after planting of the treated seed before transformation of iprodione occurs and before the seed germinates. Significant exposure, however, may occur at field edges where turning and lifting of planting equipment will lead to treated seed being left on the soil surface. This location in the field will provide birds and small mammals with potentially greater exposure to treated seed. To reduce the potential for exposure to birds and small wild mammals associated with feeding on treated seed left on the soil surface, the following statement would be proposed on seed treatment product labels:

> "Treated seed is toxic to birds and small wild mammals. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned up from the soil surface."

Terrestrial Vertebrates – granular applications

Iprodione is registered in granular form for use on golf courses to prevent various turfgrass diseases (Protuff PCP 23696). Birds and mammals may be exposed to iprodione in its granular form mainly through inadvertent ingestion of granules (in other words, granules adhered to selected food or picked up with other extraneous material during feeding) and mistaking granules for food. A risk assessment was conducted for birds and mammals to address the intake of granules. The risk assessment method for granular pesticides is similar to that of spray applications, except that the dietary items are granules rather than food items contaminated with pesticide. Mammals are only likely to consume granules unintentionally, therefore, the actual number of granules that would be consumed is expected to be very low (mammals will not actively search out inorganic granules for consumption). Unlike mammals, birds may actively search out granules for use as grit, and therefore exposure may be relatively high.

The exposure of birds and mammals to a pesticide through consumption of granules is a function of the amount of pesticide contained within the granule, the body weight and food ingestion rate of the animal and the number of granules available for consumption. For the screening level assessment, it is assumed that the bird and mammal diets will consist 100% of treated granules and that the granules are available *ad libitum*, over an extended time period.

The risk was assessed using the same generic bird and mammal body weights and toxicity endpoints selected for use in the foliar application and seed treatment risk assessment. These endpoints were converted to the number of granules needed to be consumed per day to reach the toxicity endpoint for each of the small, medium and large size classes of birds and mammals (shown in Appendix VIII, Table 10). The number of granules consumed per day calculated for each bird and mammals body weight categories is presented in Appendix VIII, Table 11. To assess the risk to birds and mammals from consumption of treated granules, a risk quotient is calculated as:

# of granules consumed per day (Appendix VIII, Table 11) ÷ # of granules to endpoint (Appendix VIII, Table 10)

The calculated risk quotients are listed in Appendix VIII, Table 12. Risks were found for all birds and mammals.

The calculation of the risk quotients assumes a highly conservative worst case scenario (in other words, 100% of the granules consumed by birds and mammals are treated granules). For birds, a more realistic exposure estimate can be used by considering the number of grit particles consumed in different bird species as well as the preferred size distribution of grit particles for different bird species. Luttik and deSnoo, 2004,[9] examined the number and size distribution of particles found in 27 species of birds. The particle size of granules reported by the registrant for Proturf (PCP 23494) is 0.726mm. The average number of particles found in birds in the 0.5 – 0.75 mm size range, ranges from 1 to 45 particles for small birds (< 50 g), up to 823 particles for medium sized birds (50 – 1000 g) and up to 9999 for large birds (>1000 g). Based on results from Luttik and deSnoo (2004), the number of grit particles 0.5 to 0.75 mm in size consumed by many species of birds is less than the number of granules required to reach avian acute or reproductive toxicity endpoints.

As it is unlikely that birds would consume, on a daily basis, high enough numbers of particles of this size to cause toxic effects, the risk assessment remains conservative. Exposure to iprodione from the ingestion of granules, therefore, is not expected to pose a risk to birds.

Small mammals are only likely to consume a granule unintentionally, therefore, the actual number of granules that would be consumed is expected to be very low (in other words, small mammals will not actively search out inorganic granules for consumption). The exposure value for mammals may then be further characterized as a low percentage of the EDE based on consumption as food (in other words, 1 - 5% of the EDE based on consumption as food). Risk quotients for mammals based on an estimate of incidental consumption as 1% of the EDE are shown in Appendix VIII, Table 13. For small mammals eating only 1% of the estimated daily exposure for granule ingestion, the risk quotients do not exceed the LOC for any effects. Exposure to iprodione from inadvertent ingestion of granules, therefore, is not expected to pose a risk to mammals.

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[9] Luttik, R. and G.R. de Snoo (2004). Characterization of grit in arable birds to improve pesticide risk assessment. Ecotoxicology and Environmental Safety 57: 319-329.

4.2.2 Effects on Aquatic Organisms

A summary of aquatic toxicity data is presented in Appendix VIII, Table 3.

Screening Level Assessment

The initial conservative screening level assessment considered the lowest single and highest cumulative crop application rates (alfalfa -1612 g a.i./ha and raspberry – 1000 g a.i./ha × 8 at 7-d intervals) based on direct application to water bodies with a depth of 15 cm (seasonal water body for amphibian endpoints) and 80 cm (permanent water body for remaining endpoints), as well as at the highest cumulative application rate for turf use (9000 g a.i./ha × 3 at 14-d intervals) at the same water depths. The aquatic EECs for cumulative application rates were conservatively estimated by adjusting the sum of the applications for dissipation between applications using a DT_{50} of 6.1 days (whole system) which is the most conservative value reported from the aerobic aquatic biotransformation studies.

Screening level EECs for the transformation product RP 30228 in 80 and 15 cm deep water bodies were determined by assuming 100% conversion of iprodione to the transformation product, and correcting for molecular weight. An estimate of the DT_{50} for RP30228 could not be determined because the parent aerobic aquatic biotransformation studies were of insufficient duration to fully track the rate of RP30228 dissipation. The initial cumulative EECs for RP30228 in water, therefore, were calculated with the assumption that RP30228 is stable.

For the assessment of risk, toxicity endpoints chosen from the most sensitive species tested were used as surrogates for the wide range of species that can be potentially exposed following treatment with iprodione. The endpoints were derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates, and by a factor of 10 for fish and amphibians. In order to assess the risk to amphibians to iprodione and RP30228, the endpoint values for the most sensitive fish was used as surrogate data.

The screening level risk quotients for acute exposure to iprodione indicate that the level of concern (LOC) is exceeded at the highest cumulative application rate for crops and turf use for freshwater invertebrates (RQ = 1.9 and 12, respectively) and marine algae (RQ = 1.4 and 8.5, respectively). The acute LOC is exceeded for fish at the cumulative application rate for turf only (RQ = 4.5). For amphibians and freshwater algae, the acute LOC is exceeded at all iprodione application rates (RQ = 1.6 – 24 and 3.8 – 58, respectively). The risk quotients determined for acute exposure to RP30288 indicate that the level of concern (LOC) is exceeded for fish and amphibians at all application rates (RQ = 1.6 – 61 and 9.1 – 327, respectively).

The screening level risk quotients for chronic exposure indicate that the LOC is exceeded at the highest cumulative application rate for crops and turf use for freshwater invertebrates (RQ = 1.4 and 8.3, respectively), for fish at the cumulative application rate for turf use (RQ = 5.4) and for amphibians and marine invertebrates at all iprodione application rates (RQ = 1.9 – 29 and 26 – 400, respectively). The risk quotients for chronic exposure to RP30228 exceed the LOC for sediment dwelling invertebrates at the highest cumulative application rates for agricultural crops and turf use (RQ =10 and 34, respectively).

Spray drift risk assessment

The risk to aquatic organisms was further characterized by taking into consideration the concentrations of iprodione that could be deposited in off-field aquatic habitat that are downwind and directly adjacent to the treated field through spray drift. Review of the labels for iprodione-containing end-use products indicate that the end-use products are applied by a variety of application methods. The maximum amount of spray that is expected to drift 1m downwind from the application site during spraying using field sprayer and aerial application methods is determined based on a fine spray droplet size: field sprayer – 11%, aerial – 26%. The maximum amount of spray that is expected to drift 1m downwind from the application site during spraying using airblast application is 74% and 59% for early and late application, respectively. The assessment of potential risk from drift was assessed for the highest cumulative application rate specific to each of the three application methods for agricultural use (ground: strawberries – 1000 g a.i./ha × 2 applications at 14 day intervals, aerial: snap beans – 750 g a.i./ha × 2 applications at 7 day intervals, airblast: raspberry – 1000 g a.i./ha × 8 applications at 7 day intervals) and the highest cumulative application rate for turf (9000 g a.i./ha × 3 applications at 14 day intervals).

The risk to aquatic organisms resulting from spray drift is summarized in Appendix VIII, Table 15. The risk quotients indicate that the LOC for acute effects in algae is exceeded for aerial, airblast and turf uses (RQ = 1.3 – 7.0), in amphibians for airblast and turf uses (RQ = 2.9 and 1.4, respectively), freshwater invertebrates and marine algae for airblast use (RQ = 1.4 and 1.0, respectively). On a chronic basis, the RQs indicate that the LOC is exceeded for amphibians for airblast and turf uses (RQ = 3.5 – 1.7) and marine/estuarine invertebrates for all application methods (RQ = 4.0 – 48).

The screening level risk assessment also indicated that the transformation product RP30228 may pose a chronic risk to freshwater sediment dwelling invertebrates and an acute risk to fish and amphibians from direct application of iprodione to water. The risk of RP30228 to these aquatic organisms was further characterized by taking into consideration the exposure concentration of RP30228 in aquatic systems that would result from iprodione received in spray drift. EECs for RP30228 were determined assuming 100% conversion of iprodione to the transformation product, and correcting for molecular weight. An additional factor was applied for the calculation of RP 30228 EECs based on evidence from aerobic aquatic biotransformation studies conducted with iprodione. The maximum whole system concentration of RP 30228 observed in the studies is 79%; the majority of RP 30228 is shown to partition into sediment. The EECs for RP30228, therefore, were multiplied by an additional factor of 0.8 to approximate the maximum concentration of RP30228 that would potentially be present in an aquatic system after receiving iprodione in spray drift.

The risk quotients for RP30228 indicate that the acute LOC is exceeded for freshwater fish for airblast and turf use (RQ = 2.5 and 1.2, respectively) and for amphibians for all application methods and uses (RQ = 1.1 - 13). On a chronic basis, the LOC is exceeded in sediment dwelling invertebrates for airblast use (RQ = 1.4). There is, however, uncertainty associated with the risk assessment for aquatic organisms exposed to RP30228. The chronic toxicity endpoint for the sediment dwelling organism, *Chironomus riparius*, is a no effect concentration determined from a limit test (in other words, a single RP30228 exposure concentration). As this study does not establish an exposure concentration at which effects occur, the use of the endpoint value derived from the study may be overly conservative for the risk assessment.

Although the results of the spray drift assessment indicate that agricultural applications of iprodione may pose a risk to aquatic organisms, the assessment may be overly conservative because the EECs for iprodione in water are based on the highest cumulative application rate and shortest interval for each of the application methods, (in other words, ground: strawberries – 1000 g a.i./ha × 2 applications at 14 day intervals, aerial: snap beans – 750 g a.i./ha × 2 applications at 7 day intervals, airblast: raspberry – 1000 g a.i./ha × 8 applications at 7 day intervals). For the purpose of managing disease resistance to iprodione, all agricultural end-product labels recommend rotating with fungicides having different modes of action. The typical number of applications reported by the registrant for iprodione on agricultural crops with the highest application rates is one application per year. Therefore, the risk of iprodione to aquatic organisms from spray drift would be expected to be lower under typical agricultural use conditions. Based on the single highest application rate for each of the agricultural methods, however, the LOC remains exceeded for acute effects in freshwater algae and amphibians for airblast use (RQ = 3.9 and 1.6, respectively) and for chronic effects in estuarine and marine invertebrates for all agricultural methods (RQ = 2.1 – 27) and in amphibians for airblast use (RQ = 1.8). For RP30228, the LOC remains exceeded for acute effects in freshwater fish for airblast use (RQ = 1.3) and amphibians for aerial and airblast uses (RQ = 1.6 and 7.2, respectively).

For turf use, the highest curative turf application rate (9000g a.i./ha) for control of snow mould was considered for the aquatic risk assessment at the screening level and for the spray drift assessment; as the number of applications per season for the control of snow mould is not clearly stated on product labels, three applications was chosen based on the maximum seasonal application rate per year supported by the registrant for all turf diseases listed on product labels (27000 kg a.i./ha). Based on information provided on some product labels and general turfgrass management recommendations (for example, OMAFRA Publication 384, 2005), application of iprodione for control of snow mould is made in late fall or early winter just prior to ground freezing or before the first snowfall, and may be repeated in mid-winter when turf is free of snow and again immediately after the final snow melt in early spring. Given that iprodione is unlikely to be applied 3 times at the highest curative rate for snow mould control, the EECs determined for turf use (9000 g a.i./ha × 3 applications) are considered highly conservative. Iprodione can also be applied to turf in the spring and summer for the control of other diseases at lower rates ranging from 1500 to 3042 g a.i./ha for preventative application rates and 4576 – 6250 g a.i./ha for curative application rates; applications to turf are typically alternated with other fungicides having different mode of action. Nevertheless, over the preventative and curative rate range for a single application, the LOC for acute effects remains exceeded in freshwater algae at curative rates (RQ = 1.4 – 2.0) and for chronic effects in estuarine and marine invertebrates at preventative and curative rates (RQ = 3.2 – 13). For RP30228, the LOC for acute effects is exceeded in amphibians over the preventative and curative rate range (RQ = 0.9 – 3.6).

The overall results of the spray drift assessment indicate that iprodione and the transformation product RP30228 may pose a risk to aquatic organisms. Buffer zones would reduce the potential risk to aquatic species.

Run-off risk assessment
Aquatic organisms can also be exposed to iprodione from foliar applications as a result of runoff into a body of water. The linked models PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modeling System) were used to predict estimated environmental concentrations (EECs) resulting from runoff of iprodione following application. Two sets of PRZM/EXAMS runs were conducted. The use on turf was simulated with weather data from five cities across Canada. In addition, four crops (raspberries in BC, beans in the Prairies, onions in ON/QC, and strawberries in the Atlantic region) with lower application rates were modelled. The iprodione EECs of all selected runs for the use pattern on turf and crops is reported in Appendix VIII, Tables 16-17, respectively for an 80 cm deep water body and a 15 cm deep water body. The values reported by PRZM/EXAMS are 90th percentile concentrations of the concentrations determined at a number of time-frames including the yearly peak, 96-hr, 21-d, 60-d, 90-d and yearly average.

Acute and chronic RQ values were calculated using an EEC for the time frame which most closely matched the exposure time used to generate the endpoint (e.g. a 96 hour LC_{50} would use the 96 hour value generated by the model; a 21 day NOEC would use the 21 day EEC value).

The acute and chronic RQ values for aquatic organisms are reported in Table 19 (Appendix VIII). The RQs derived for acute exposure resulting from turf use, exceed the LOC for freshwater invertebrates, amphibians and freshwater algae (RQ = 1.0, 1.1 and 3.5, respectively). For crop uses, the RQs for acute exposure exceed the LOC for freshwater algae (RQ = 1.8). On a chronic basis, the RQs indicate that the LOC is exceeded marine invertebrates (turf and crop use; 8.6 and 5.4, respectively). As previously mentioned, the assessment may be overly conservative because the EECs for iprodione are based on the highest cumulative application rate and shortest interval for each of the runoff scenarios modeled. For the purpose of managing disease resistance to iprodione, all agricultural end-product labels recommend rotating with fungicides having different mode of action. The risk of iprodione to aquatic organisms from runoff, therefore, would be expected to be reduced under typical agricultural and turf use conditions.

EECs for the transformation product RP30228 from runoff were not modelled due to a lack of environmental fate data (e.g. aerobic aquatic biotransformation half-life). Therefore, an aquatic risk assessment based on runoff of RP30228 could not be conducted.

4.2.3 Endocrine Disruption Potential

Mammalian toxicity studies have indicated that chronic dietary exposure to iprodione resulted in testicular hyperplasia and reduced spermatozoa in the epididymis of rats. Altered parental behaviour and reduced embryo survival were observed in avian reproduction studies. Aquatic toxicity studies indicate effects on reproduction in both fish and invertebrates. Whether the non-mammalian test results reflect the ability of iprodione to act on endocrine-mediated processes is uncertain. Additionally, iprodione has a structure similar to that of vinclozolin, an antiandrogenic compound; however, there is uncertainty regarding the extent to which iprodione may act through a similar mode of action.

Iprodione is listed as an endocrine disrupter in the *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis,* USEPA, 1997. In September 2005, the USEPA published its approach for selecting the initial list of chemicals for which testing will be required under the Endocrine Disruptor Screening Program (EDSP). The initial pesticides selected for screening in the EDSP were chosen based on 1) high production volumes and usage (agricultural and residential), and 2) potential for human exposure via food, water, residential use and occupational exposure pathways. Although selection for the list focused on human exposure, it is expected that the list will also capture many pesticides that have potential for widespread environmental exposures. In April 2009, the USEPA published the final list of the first group of chemicals proposed for screening in the Agency's EDSP; this list includes iprodione.

4.2.4 Incident Reports

Environmental incident reports are obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the USEPA Ecological Incident Information System (EIIS). If information on environmental incidents is available from other governments (for example, OECD countries) this information is also taken into consideration. Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007 under the *Pest Control Products Act* can be found at: http://canadagazette.gc.ca/partII/2006/20061115/html/sor260-e.html.

As of 20 March 2015, no Canadian incident reports have been reported. However, a total of 19 environmental incidents are reported in the USEPA EIIS database, of which 17 are listed as the result of registered labelled use. Fourteen incidents, all occurring in 2003, report damage to a hybrid variety of blueberries (rabbiteye blueberries) after application of Rovral 4F; the registrant has since amended the product label restricting use on rabiteye blueberries.

Application of iprodione to an unspecified agricultural area in California resulted in the death of honeybee brood following application of Rovral to blooming almond trees. The certainty of the bee kill incident being related to iprodione is classified as "probable".

In another bee kill incident, Rovral fungicide was reportedly applied to a cherry orchard by airblast sprayer during the evening when bees being used for pollination services were in the vicinity. Of the 80 colonies reported to be in the orchard, roughly 20% exhibited a reduction in forage force (reduced numbers of adult bees), and adult bee populations in these colonies were estimated at roughly 50%. Although spraying occurred in the evening hours, bees were likely bearding on the outside of the colonies and were directly sprayed with Rovral. The certainty of the bee kill incident being related to iprodione is classified as "probable".

The remaining incident resulting from registered use is for a fish kill located in a drainage canal adjacent to a golf course. Other pesticides listed in the report that are more toxic to fish (in other words, carbaryl, chlorpyrifos) are thought to be responsible for the incident.

5.0 Value

In Canada, iprodione is registered for the control of 24 fungal pathogens on 24 crop species, 53 ornamental species and turf including some destructive pathogens: *Botrytis cinerea* (botrytis grey mould) on raspberry and strawberry; *Sclerotinia sclerotiorum* (Sclerotinia stem rot/white mould) on canola and dry common and snap beans, *Monilinia fructicola* (brown rot/blossom blight) on stone fruits, *Rhizoctonia solani* (Rhizoctonia stem and stolon canker) on potato, and *Sclerotinia homoeocarpa* (dollar spot), *Colletotrichum cereale* (basal rot anthracnose), *Rhizoctonia solani* (brown patch) and *Typhula* spp. and *Microdochium nivale* (grey and pink snow moulds), *Fusarium nivale* (fusarium patch) on turf. Sites with the largest amount of annual usage of iprodione are canola for the control Sclerotinia stem rot and Alternaria black spot, and turf particularly for snow mould control.

Canola Diseases
Iprodione is registered for use on canola as a foliar treatment for the control of Sclerotinia stem rot and Alternaria black spot, and as a seed treatment for the control of Rhizoctonia damping-off and root rot, seed-borne blackleg and Alternaria black spot on emerging canola seedlings. Sclerotinia stem rot is a major disease of canola and has the potential to reduce yields by half under severe conditions. Although Alternaria black spot is classified as a minor disease, it is widespread in Western Canada. Yield loss greater than 20% with heavy infection on the pods is not uncommon in the Western provinces.

A very large proportion of the canola grown in Canada is treated with iprodione by foliar applications against Sclerotinia stem rot and Alternaria black spot. Registered chemical alternatives to iprodione as of 27 April 2015 and their limitations for use on canola for the control of Sclerotinia stem rot are listed in the following table:

Active ingredients	Group	Comments
Azoxostrobin	11	At high risk for resistance development. Resistance management required. Cross resistance is present between all members of Group 11 fungicides.
Picostrobin	11	
Pyraclostrobin	11	
Boscalid	7	At medium to high risk for resistance development. Resistance management required. The Group 7 fungicides are in general cross-resistant.
Fluxapyroxad	7	
Penthiopyrad	7	
Isofetamid	7	
Metconazole	3	At medium risk for resistance development. Resistance management is required. Cross resistance is present between Group 3 fungicides active against the same pathogen.
Prothioconazole	3	
Cyprodinil	9	At medium risk for resistance development. Resistance management required .
Fludioxonil	12	At low to medium risk. Resistance management required .

In addition to the chemical alternatives, two biofungicides, *Coniothyrium minitans* strain CON/M/91-08 and *Bacillus subtilis* strain QST 713 are registered for suppression of Sclerotinia stem rot on canola; however, they are somewhat limited as alternatives to iprodione due to their lower level of control.

The registered alternatives to iprodione for Alternaria black spot control are azoxystrobin and pyraclostrobin (Group 11), boscalid and fluxapyroxad (Group 7) and a pre-mix product of fluxapyroxad and pyraclostrobin. Cross resistance between members belonging to the same MoA group is present in populations of the same pathogen, therefore, growers have a limited number of effective alternative active ingredients for resistance management and control of Alternaria black spot.

Turf Diseases

Iprodione is among the important fungicides for the control of turf diseases since it consistently provides good to excellent control of the important turf diseases, pink snow mould (Fusarium patch), grey snow mould, dollar spot, leaf spot/melting out, rust diseases and brown patch on turf. Grey and pink snow mould fungi are active from late fall to early spring. Preventative application of fungicides is recommended just before snowfall to control snow moulds. An alternative product, Instrata (PCP No. 28861), formulated with three active ingredients: fludioxonil, propiconazole and chlorothalonil, provides season-long control of both pink and grey snow moulds with only one application in the fall. Fludioxonil and chlorothalonil are currently under re-evaluation.

The other chemical alternatives to iprodione for snow moulds control include azoxystrobin, fluoxystrobin, pyraclostrobin and trifloxystrobin (all in Group 11); propiconazole, triticonazole and myclobutanil (all in group 3) and thiophanate-methyl (Group 1). Myclobutanil has the disadvantage of only controlling grey snow mould.

Thiophanate-methyl is registered for control of pink snow mould and is currently under re-evaluation. All group 11 fungicides are at high risk for resistance development, therefore resistance management is required. In addition, cross-resistance occurs between all members of this group.

Resistance Management

Iprodione has been registered in Canada for use in agriculture, horticulture and turf for over 30 years. Dicarboximide fungicides (such as iprodione) were originally introduced in the 1970s for the control of grey mould (*Botrytis cinerea*) on grapes as an alternative to the benzimidazole fungicides, to which resistance had developed in several countries including Canada. The lack of good resistance management practices and overuse of this active ingredient meant resistance to iprodione also developed quickly in *B. cinerea* in some areas. Despite the widespread development of resistance in *B. cinerea*, iprodione still provides effective control of other important plant diseases on many crops including canola and turf.

Iprodione is effective in two ways: (i) as a contact fungicide, it inhibits the growth and development of the target pathogen, and (ii) as a fungicide with curative action, it also inhibits the growth of the target pathogen even after establishment. Iprodione is best regarded as a protectant fungicide. Because of these properties, although resistance to iprodione has been detected in isolates of some fungal pathogens particularly in *B. cinerea*, it is still effective in integrated pest management (IPM) programs in areas where resistance is not present and for diseases other than grey mould as a tank-mix partner or as a rotational fungicide with other fungicide active ingredients that are at high risk for resistance development.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances which meet all four criteria outlined in the policy:persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*.

During the review process, iprodione and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[10] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Iprodione does not meet all Track 1 criteria, and is not considered a Track 1 substance. See the table below for comparison with Track 1 criteria.
- Iprodione does not form any transformation products that meet all Track 1 criteria.

Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	**TSMP Track 1 Criterion value**		**Iprodione Are criteria met?**
Toxic or toxic equivalent according the *Canadian Environmental Protection Act*[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	No: 16.3 – 83.8 days
	Water	Half-life ≥ 182 days	No: 0.3 – 0.6 days
	Whole system (Water + Sediment)	Half-life ≥ 365 days	No: 6.1 days
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilization is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (2.7×10^{-7} mm Hg) and Henry's Law Constant (9.02×10^{-9} atm m^3/mole).
Bioaccumulation[4]	Log $K_{OW} \geq 5$		No: 3.1
	BCF ≥ 5000		not available
	BAF ≥ 5000		No: 72 x
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			**No, does not meet all TSMP Track 1 criteria.**

[1] All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).

[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

[4] The log L_{OW} and/or BCF and/or BAF are preferred over log K_{OW}.

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[10] DIR99-03, The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[11] The list is used as described in the PMRA Notice of Intent NOI2005-01[12] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[13], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade iprodione and its end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

7.0 Organisation for Economic Co-operation and Development Status of Iprodione

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups member countries and provides a forum in which governments can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member country to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Iprodione is currently acceptable for use in other OECD countries, including the United States, Australia and the European Union Member States. As of 11 September 2015, no decision by an OECD member country to prohibit all uses of iprodione for health or environmental reasons has been identified.

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[11] *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

[12] NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* under the New *Pest Control Products Act*.

[13] DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

8.0 Summary

8.1 Human Health and Safety

The toxicology database submitted for iprodione characterized the toxic effects which may result from exposure. Iprodione is of slight or low acute toxicity by the oral, dermal or inhalation route, mildly irritating to the eye and not a skin irritant or sensitizer. The target organs of toxicity were the liver and endocrine system. Iprodione caused tumours in rats and mice following prolonged oral exposure. No sensitivity of the young was observed in the toxicity database although numerous reproductive and developmental endpoints were affected. The risk assessment takes these and any other potential effects into account in determining the allowable level of human exposure to iprodione.

8.1.1 Dietary Risk (Food Only)

Acute and chronic exposure from iprodione in food alone was below the ARfD and ADI for all population groups and is not of concern.

The lifetime cancer risk for food alone was determined to be 1×10^{-6} for the general population and is not of concern. However, the cancer risk did reach the benchmark of 1×10^{-6}. Residues in imported peaches, nectarines, and other stone fruits were the major exposure and risk contributors in the assessment.

8.1.2 Dietary Risk (Food and Drinking Water)

Food and drinking water exposure estimates were determined using three different EECs based on typical use rates for turf, orchard, or canola.

Acute and chronic exposure from iprodione in food and drinking water was below the ARfD and ADI for most of the population groups and use rates assessed. However, the cancer risk exceeded 1×10^{-6} for the general population for all use rates and is of concern. The cancer risks ranged from 3×10^{-6} to 4×10^{-5}. Residues in drinking water were the major exposure and risk contributors in the food and drinking water assessment.

8.1.3 Non-Occupational Risk

There are no domestic class products registered; however, bystander exposure may occur through exposure to household dust, ambient air or golfing. Bystander exposure is not of concern based on available data.

8.1.4 Occupational Risk

For workers entering treated agricultural sites, most current label REIs are not protective. Calculated REIs range from 12 hours to 137 days. Many of the proposed REIs are not agronomically feasible.

8.1.5 Aggregate Risk (Food, Drinking Water and Non-Occupational Exposure)

An aggregate assessment for iprodione (beyond combining food and drinking water) was not conducted as risk concerns were already identified from food and drinking water.

8.2 Environmental Risk

Available studies suggest that in the natural environment, iprodione is slightly to moderately persistent in soil and non-persistent in water. Iprodione has low to medium mobility in soils with mobility shown to be reduced in soil with increasing organic matter content. When iprodione is applied to soil, it is not expected to leach into groundwater, with the possible exception of sandy soil conditions.

Risk assessments indicated that there is potential for adverse effects on foraging pollinators, beneficial insects, birds, mammals and aquatic organisms from the use of iprodione.

8.3 Value

Iprodione is registered for the control of a number of economically important fungal diseases on field, orchard and greenhouse food crops, greenhouse and outdoor ornamentals and turf. Particular sites with large use of iprodione include foliar treatments for the control of Sclerotinia stem rot and Alternaria black spot on canola, and turf diseases particularly grey and pink snow moulds. A limited number of effective alternative active ingredients to iprodione are currently available for resistance management and control of Alternaria black spot on canola.

In cases where resistance is not present, iprodione contributes to sustainable pest management and plays a role in resistance management in IPM programs where it is used as a tank-mix partner or in rotation with other fungicides that are at high risk for development of resistance.

9.0 Proposed Regulatory Re-evaluation Decision

After a re-evaluation of the fungicide iprodione, Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing the cancellation of all iprodione uses based on risks associated with human health.

Additional Data Requirements Related to Health Risk Assessment

As the PMRA is proposing cancellation of all registered uses of iprodione, no additional data will be required under section 12 of the *Pest Control Products Act*. The PMRA will consider additional data submitted during the 60-day consultation period to further refine the health risk assessment, should that become available. To address the risks of concern identified in the re-evaluation, data may include the following:

- Data on the use pattern, toxicology, drinking water, occupational exposure, and residue chemistry;
- Data to address gaps in the 3,5-dichloroaniline (3,5-DCA) health risk assessment.

It is recommended that registrants interested in submitting additional data during the 90 day consultation period first consult with the Agency.

List of Abbreviations

↑	increased
↓	decreased
µg	micrograms
µL	microlitre
♀	female
♂	male
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
abs	absolute
ADD	Absorbed Daily Dose
ADI	allowable daily intake level
AHETF	Agricultural Handler Exposure Task Force
ALP	alkaline phosphatase
ALT	alanine transaminase
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
AST	aspartate transaminase
atm	atmosphere
ATPD	area treated per day
BAF	bioaccumulation factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
BWG	body weight gain
°C	degree Celsius
CAF	composite assessment factor
cAMP	cyclic adenosine monophosphate
CAS	chemical abstracts service
CFIA	Canadian Food inspection Agency
cm	centimetre(s)
d	day(s)
DA	dermal absorption
DACO	data code
DAT	days after treatment
DEEM-FCID	dietary exposure evaluation model – food consumption intake database
DER	data evaluation report
DFR	dislodgeable foliar residue
DHT	dihydrotestosterone
DNT	developmental neurotoxicity study
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{75}	dissipation time 75% (the time required to observe a 75% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
dw	dry weight

EC	emulsifiable concentrate
EC_{05}	effective concentration on 5% of the population
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EP	end use product
ER_{25}	effective rate on 25% of the population
ER_{50}	effective rate on 50% of the population
EU	European Union
EUP	end-use product
EXAMS	exposure analysis modeling system
F0	parental generation
F1	first filial generation
F2	second filial generation
FC	food consumption
FDR	Food and Drugs Regulations
FE	food efficiency
Fg	microgram(s)
FIR	food ingestion rate
Fm	micrometre(s)
FRAC	Fungicide Resistance Action Committee
FSH	follicle stimulating hormone
g	gram(s)
GAP	good agricultural practice
GC	gas chromatography
GLC	gas liquid chromatography
GLP	good laboratory practices
GR	granular
GSD	geometric standard deviation
ha	hectare(s)
Hb	hemoglobin
Hb	hemoglobin
hCG	human chorionic gonadotropin
Hct	hematocrit
HDT	highest dose tested
HED	Health Evaluation Division
HPLC	high performance liquid chromatography
hr	hour
ILV	independent laboratory validation
IPM	intergrated pest management
IUPAC	International Union of Pure and Applied Chemistry
IV	intravenous
K_a	dissociation constant
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
kg	kilogram(s)
K_{oc}	organic-carbon partition coefficient

K_{ow}	octanol-water partition coefficient
L	litre(s)
LADD	lifetime average daily dose
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LDT	lowest dose tested
LEACHM	leaching estimation and chemistry model
LH	luteinising hormone
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
M/L/A	mixer/loader/applicator
MAP	mitogen-activated protein
mg	milligram(s)
mL	millilitre(s)
MMAD	mass median aerodynamic diameter
MOA	mode of action
MOE	margin of exposure
MOR	magnitude of residue
MRL	maximum residue limit
MRM	multi-residue method
MS	mass spectrometry
MTD	maximum tolerated dose
mth(s)	month(s)
N/A	not applicable
N/R	not required
N/S	not specified
ND	not determined
NM	not measured
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OC	organic carbon content
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
ORETF	outdoor residential exposure task force database
Pa	pascal
PAM	pesticide analytical manual
PBI	plant back interval
PCP	pest control product
PCT	percent crop treated
PDP	Pesticide Data Program
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency

PPE	personal protective equipment
ppm	parts per million
PRVD	proposed re-evaluation decision
PRZM	pesticide root zone model
PYO	pick your own facilities
q_1^*	cancer unit risk
RBC	red blood cells
RD	residue definition
REI	restricted entry interval
rel	relative
RfD	reference dose
RSD	relative standard deviation
RVD	re-evaluation decision
SG	soluble granule
SN	solution
SO	solid
SU	suspension
$t_{1/2}$	half-life
TC	transfer coefficient
TGAI	technical grade active ingredient
TLC	thin layer chromatography
TRR	total radioactive residues
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
URMULE	use requested minor use label expansion
USEPA	United States Environmental Protection Agency
USC	use site category
UV	ultraviolet
v/v	volume per volume dilution
WC	water consumption
WG	wettable granules
wk	week(s)
WSP	wettable granules in water soluble package
wt	weight

Appendix I Iprodione Products Registered in Canada as of 27 April 2015, Excluding Discontinued Products or Products with a Submission for Discontinuation

Regn No	Marketing Class	Registrant	Product Name	Formulation	Multiple / Single Active Ingredients	Guarantee (iprodione)
29379	Technical	ADAMA AGRICULTURAL SOLUTIONS CANADA LTD.	QUALI-PRO IPRODIONE TECHNICAL	SOLID	Single	99%
20267		FMC CORPORATION	IPRODIONE TECHNICAL	Not Specified	Single	98.6%
29410	Commercial	ADAMA AGRICULTURAL SOLUTIONS CANADA LTD.	QUALI-PRO IPRODIONE 240 SE	SUSPENSION	Single	240 g/L
30275			OVERALL 240 SC	SUSPENSION	Single	240 g/L
23494		AGRIUM ADVANCED TECHNOLOGIES RP INC.	PROTURF GRANULAR FUNGICIDE X CONTAINING IPRODIONE	GRANULAR	Single	1.3%
24379		BAYER CROPSCIENCE INC.	GREEN GT	SUSPENSION	Single	240 g/L
29870			TRILOGY SC	SUSPENSION	Multiple	29.41%
30534			IPRODIONE TURF AND ORNAMENTAL FUNGICIDE	WETTABLE POWDER	Single	500 g/kg
15213		FMC CORPORATION	ROVRAL FUNGICIDE WETTABLE POWDER	WETTABLE POWDER	Single	500 g/kg
24378			ROVRAL RX FUNGICIDE CONTAINS IPRODIONE	SUSPENSION	Single	240 g/L
24709			ROVRAL® WDG FUNGICIDE WATER DISPERSABLE GRANULE	WETTABLE GRANULES	Single	500 g/kg
29315			ROVRAL FLO FUNGICIDE	SUSPENSION	Single	240 g/L
29866			ID FUNGICIDE	SUSPENSION	Single	240 g/L
28525		NIPPON SODA COMPANY LTD.	NISSO FOUNDATION LITE	SUSPENSION	Multiple	132 g/L

Appendix II Commercial Class Uses of Iprodione Registered in Canada, Excluding Uses of Discontinued Products or Products with a Submission For Discontinuation as of 27 April 2015

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum Number of Applications per Year	Typical Number of Days Between Applications
				Maximum Single	Maximum Cumulative		
Use-site Category 5: Greenhouse Food Crops							
Lettuce	Grey mould/Sclerotinia drop	Wettable powder, wettable dispersible granules	Ground application: foliar spray - high volume sprayer	1000	(4000)	[4]	7-10
Cucumber	Gummy stem blight		Ground application: foliar spray	[1000]	(4000)		7
	Botrytis grey mould						
Tomato				[625]	(2500)		
Use-site Category 6, 27: Greenhouse Non-Food Crops, Ornamentals Outdoor							
Conifer seedlings (spruce, fir, hemlock and cedar) - container or bareroot conifer seedlings in greenhouses and conifer nurseries	Botrytis blight	Wettable powder, wettable dispersible granules	Ground application: foliar spray	1000	3000	3	21
Ornamentals[1]	*Botrytis* spp.		Ground application: foliar spray	5 g/ 10 L	Can not be calculated	[4]	21
Ornamentals - Celosia, Salvia	Damping-off (*Rhizoctonia* spp.)		Ground application: Drench (watering equipment)	10 000 (1 g / m^2)	(20 000)	[2]	Not stated

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum Number of Applications per Year	Typical Number of Days Between Applications
				Maximum Single	Maximum Cumulative		
Use-site Category 13. Terrestrial Feed Crops							
Alfalfa grown for seed (Saskatchewan, Alberta, Manitoba and the Peace River region of British Columbia)	Sclerotinia (*Scleretonia sclerotiorum*)	Suspension	Ground application: foliar spray – boom sprayer	744	744	1	Not applicable
Use-site Category 7, 13, 14: Industrial Oil Seed Crops and Fibre Crops, Terrestrial Feed Crops, Terrestrial Food Crops							
Canola	Sclerotinia stem rot	Wettable powder, wettable dispersible granules, suspension	*Ground and aerial: foliar spray – boom sprayer*	750	(750)	[1]	Not applicable
	Alternaria black spot			504	(504)		
Use-site Category 10: Seed Treatments Food and Feed							
Canola	Damping off and root rot caused by *Rhizoctonia solani*, seed borne blackleg and seed borne Alternaria black spot on emerging seedlings	Suspension	Ground application: Seed treatment equipment commercial and on farm (open and closed systems)	23.76	23.76	1	Not applicable
Mustard				33.26	33.26		
Garlic	Green mould (*Penicillium corymbiferum*)	Wettable powder, wettable dispersible granules	Ground application: Seed treatment - dip	2 g/L	Cannot be determined		
Carrot	Seed borne Alternaria	Wettable powder	Seed is treated prior to import into Canada	260.5 g/100 kg seed (~ 11.72 g/ha, based on 4.5 kg seed /ha for fresh market carrots)			

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum Number of Applications per Year	Typical Number of Days Between Applications
				Maximum Single	Maximum Cumulative		
Use-site Category 30: Seed Treatments Food and Feed							
Potato	Rhizoctonia stem and stolon canker, silver scurf – suppression	Suspension	Ground: Potato seed piece treatment equipment (open and closed systems)	10.08 g/100 kg seed pieces = 406.7 g / ha for seed potato (Based on 4035 kg seed pieces / ha at 15 cm in-row spacing)) and = 129.9 to 203.41g / ha for table and processing potato, respectively (Based on 1289 kg / ha seed pieces at 46 cm in-row spacing and 2018 kg / ha seed pieces at 31 cm in-row spacing)	406.7 g / ha for seed potato and 129.9 to 203.41 g / ha for table and processing potato	1	Not applicable
Use-site Category 14: Terrestrial Food Crops							
Grapes	Botrytis bunch rot	Wettable powder, wettable dispersible granules	Ground application: foliar spray – boom and airblast sprayer	750	1500	2	(7-14)
Lettuce, field (head & leaf)	Grey mould		Ground application: foliar spray – boom sprayer	750	3000	4	7
Dry common beans (white and kidney)	Sclerotinia white mould			750	(1500)	(2)	(7)
Ginseng	Alternaria leaf blight			750	2250	3	10
Use-site Category 14: Terrestrial Food Crops							
Snap beans	Sclerotinia white mould, Botrytis pod rot (normally only a problem in British Columbia)	Wettable powder, wettable dispersible granules	Ground and aerial application: foliar spray	750	1500	2	Not stated
Raspberry	Grey mould fruit rot	Wettable powder, wettable dispersible granules	Ground and aerial application: foliar spray – boom sprayer and airblast	1000	4000	4	7-10
Strawberry	Botrytis fruit rot, Penicillium spp. (suppression)		Ground and aerial application: foliar spray – boom sprayer	1000	(2000)	(2)	7-10
Plum/prune	Brown rot		Ground and aerial application:	750	(1500)	(2)	7-14

Host	Pest	Formulation Type	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum Number of Applications per Year	Typical Number of Days Between Applications
				Maximum Single	Maximum Cumulative		
Cherry (sweet)			Foliar spray – airblast sprayer	[illegible]	(1750)		
Peach							
Apricot	Brown rot/blossom blight			750	(1500)		
Cauliflower	Alternaria		Ground application: foliar spray – boom sprayer	1500	1500	1	Not applicable
Cabbage (stored)							
Onion (dry bulb)	Botrytis leaf blight, downy mildew			750	(3750)	[5]	7-10
Leek	Botrytis leaf blight	Wettable powder			3000	4	
Use-site Category 30: Turf							
Turf – fairways, putting greens and other turf areas including sod production consisting of Kentucky bluegrass, bentgrass, perennial ryegrass and fine fescue, or where these mixtures predominate (excluding residential turf)	Brown patch, Fusarium patch, grey snow mould, pink snow mould, leaf spot, dollar spot, red leaf spot, Rhizoctonia, *Helminthosporium* leaf spot, melting out	Wettable powder, wettable dispersible granules, suspension, granular	Ground application: foliar spray – boom sprayer	(250) – 5000	(17500) [(27000)]	[(6)]	14-21

Information in square brackets [ ] is proposed by the registrant, and information in round brackets ( ) is calculated by the PMRA.

¹These include the following ornamentals: [illegible]

Appendix III Toxicology Assessment for Iprodione

Table 1 Toxicology Endpoints for Use in Health Risk Assessment for Iprodione

Exposure Scenario	Endpoint	Value	Study/Point of Departure	CAF or MOE*
Acute Dietary (females 13-49)	Decreased anogenital *distance in fetuses*	ARfD = 0.067 *mg/kg bw*	Developmental Toxicity *Study; Rat* NOAEL: 20 mg/kg bw	300
Chronic Dietary	Increased adrenal weights and decreased in prostate weights	ADI = 0.014 mg/kg bw/day	1-yr Dog study LOAEL: 4.1 mg/kg bw/day	300
Dermal/Inhalation[2] (Short Term)	Decreased testes and prostate weights. Increased adrenal weight		13-wk Rat study NOAEL: 15 mg/kg bw/day	300
Dermal/Inhalation (Intermediate/Long Term)[2]	Increased adrenal weights and decreased prostate weights.		1-yr Dog study LOAEL: 4.1 mg/kg bw/day	300
Aggregate Short Term	Decreased testes and prostate weights. Increased adrenal weight.		13-wk Rat study NOAEL: 15 mg/kg bw/day	300
Cancer endpoint	q_1* value[2] Mouse Liver Tumours (♂) = 8.89×10^{-3} (mg/kg bw/day)$^{-1}$ [3]			

[*] - CAF (composite assessment factor) refers to the total of uncertainty and *Pest Control Products Act* factors for dietary risk assessments; MOE refers to target MOE for occupational assessments.

[2] Since an oral point of departure was selected, a dermal absorption factor 16% or inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

[3] A q_1* value of 6.38×10^{-2} (mg/kg bw/day)$^{-1}$ for 3,5-dichloroaniline was also used in the assessment based on rat hemangiosarcomas (spleen).

Table 2 Toxicology Profile for Iprodione

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute and relative organ to bodyweights unless otherwise noted.

Study/Species/ PMRA #	Results/Effects
Metabolism/Toxicokinetic Studies	
Oral studies (gavage) conducted in the rat with iprodione radiolabelled with ^{14}C (PMRA 1231370, 1166139, 1220704, 1220703) **Absorption:** Iprodione was readily absorbed after a single oral dose (50 or 900 mg/kg bw). At the low dose, blood levels peaked at 2 and 4hrs in ♂ and ♀, respectively, whereas at the high dose, blood levels peaked at 6 hrs in both sexes and were ≈ 3x greater than with the low dose. **Distribution:** After 14 days of repeat dosing with 50 mg/kg bw, individual tissue concentrations were < 1 ppm 168 hours post-dose. Individual tissue concentrations were < 0.7 ppm in both sexes following a single dose of 50	

Study/Species/ PMRA #	Results/Effects
mg/kg bw and < 10 ppm with a single dose of 900 mg/kg bw at 168 hours post-dose. Collectively, ~0.3% of the radioactivity was found in tissues with the highest concentrations noted in liver and intestines. Tissues sampled 4 days after a single oral dose of 100 mg//kg bw contained about 1% of the administered radioactivity. Highest levels were found in the skin (0.5%) and liver (0.9-0.1%). **Metabolism:** Iprodione biotransformation included hydroxylation of the aromatic ring (RP 36120), dealkylation and degradation of the isopropylcarbamoyl chain (RP 32490) and rearrangement followed by cleavage of the hydantoin moiety (RP 36115, RP 36114). Molecular rearrangement also resulted in iprodione isomers and intermediate metabolites. Iprodione was extensively metabolized regardless of dose. Overall, metabolites detected in the urine included iprodione, RP 32490, RP 36112, RP 36114, RP 36115, RP 36116, RP 36118 and RP 36119 and RP 25040. The most abundant metabolites detected in the urine were RP 32490 and RP 36114. ≈10-20% of the radioactivity in urine was not identified. ♀ eliminated more of the parent compound in the urine than the ♂. The faeces contained the same metabolites as urine, as well as RP 25040, RP 36113 and RP 30228. The most common compounds in the faeces included unchanged iprodione (30 % of the low and 80% of the high dose), RP 36115/36119, RP 32490 and RP 36114. ≈20-45% of the radioactivity in faeces was not identified. Overall, the principal metabolic products were metabolites with degraded isopropylcarbamoyl groups, generated by N-dealkylation or hydrolysis of the Co-N bonds in iprodione (RP 32490, RP 25040) and the hydroxylated benzene ring metabolite (RP 36114). **Elimination**: Elimination of iprodione was rapid, with 90 to ~100% eliminated within 2-4 days, depending on the dose. The balance between urinary and faecal excretion shifted towards urinary excretion at lower doses and faecal excretion at higher doses. ♂ may have absorbed more of the dose than ♀, based on greater urinary excretion. The high dose appeared to be absorbed to a lesser extent than the low dose, based on ↑ faecal excretion. The elimination $t_{1/2}$ were ≈ 7-9 hrs at 50 mg/kg bw and ≈ 20 -13 hrs at 900 mg/kg bw, where elimination appeared slower in ♂ than in ♀ rats. A dermal absorption study (supplemental) was conducted in rats with 185 mg ^{14}C-iprodione/kg bw (PMRA 1220773) **Metabolism:** Unaltered iprodione was found in the urine, faeces and intestines. Metabolite RP 32490 was found in urine, RP 36114 in urine, faeces and intestines and RP 30228 in urine of ♂ only.	
Acute Toxicity Studies	
Acute oral toxicity CD-1 *mouse* PMRA - 1711132	LD_{50} = 1870/ 2670 mg/kg bw (♂/♀) ≥900 mg/kg bw - epiphora, decrease in muscular tension, depression, slow respiration, dyspnea and quadriplegia as well as systemic paralysis. Paralysis progressed in order of the hind legs, forelegs, and then whole body prior to death. Tonic convulsion was also noted. **Slight Toxicity**
Acute oral toxicity CD rat PMRA - 1711131	LD_{50} = 2060/1530 mg/kg bw (♂/♀) Epiphora, ↓ in muscular tension, depression, slow respiration, dyspnea, quadriplegia and systemic paralysis (paralysis progressed in order of hind legs, forelegs and then whole body) **Slight Toxicity**
Acute oral toxicity Wistar rat	LD_{50} = 3700 mg/kg bw External bleeding (nose), lacrimation, ataxia and diarrhea

Study/Species/ PMRA #	Results/Effects
PMRA - 1711129	**Low Toxicity**
Acute oral toxicity CD-1 mouse, CD rat, Beagle and common dog PMRA 1220393	LD_{50}> 2000 mg/kg bw for all species.(mouse LD_{50} = 4000 mg/kg bw, rat and dog LD_{50} > 2000 mg/kg bw) **Low Toxicity**
Acute inhalation toxicity SD rat PMRA 1128941	$LC_{50} \geq 3.29$ mg/L (4-hr whole body exposure) No deaths or adverse effects **Low Toxicity**
Acute inhalation toxicity SD Rat PMRA 1711133	$LC_{50} \geq 5.16$ mg/L (4-hour exposure) **Low Toxicity**
Acute dermal toxicity CD rat, NZW rabbit PMRA 1220393	Rat LD_{50}> 2500 mg/kg bw: no effects on mortality, clinical signs or macroscopic observations, ↓ BWG after 5 days in ♂ Rabbit LD_{50}> 1000 mg/kg bw: no effects on mortality, clinical signs, BWG **Low Toxicity**
Acute dermal toxicity NZW rabbit PMRA 1611937	LD_{50} > 2000 mg/kg **Low Toxicity**
Acute dermal toxicity Rabbit PMRA 1611922	LD_{50} > 30,000 mg/kg **Low Toxicity**
Eye irritation NZW rabbit PMRA 1611925	Corneal injury resolving by 72 hrs. Conjunctival irritation resolved by day 7 **Mild eye irritant**

Study/Species/ PMRA #	Results/Effects
Eye irritation NZW rabbit PMRA 1611923	Conjunctival effects resolved by day 7 Supplemental
Eye irritation NZW rabbit PMRA 1220393	Non irritating to the eye
Dermal irritation NZW rabbit PMRA 1128942	**Not a dermal irritant**
Dermal Sensitization Guinea Pig PMRA 1128943	**Not a dermal sensitizer** via Buehler method.(Concentration: 10% for induction and challenge, 5% for re-challenge)
Subchronic Toxicity Studies	
4-week dietary toxicity CF-1 mouse PMRA 1816255	**NOAEL = 390/420 mg/kg bw/day (1900 ppm)** ≥950/ 1000 mg/kg bw/day (6000 ppm): ataxia and lethargy during 1st week. ↑ liver wt, stippled appearance of liver, ↑ hepatocyte vacuolation and focal eosinophilic degeneration 2300/2400 mg/kg bw/day (15000 ppm): mortality, ↓ BWG and FC. Granulomatous inflammation observed in the heart, liver and kidney (possibly in response to a foreign body)
4-week dietary toxicity CF-1 Carworth mouse PMRA 1816255	**NOAEL = 366/439 mg/kg bw/day (1900 ppm)** ≥ 366/439 mg/kg bw/day (1900 ppm): white liver foci (non-adverse) ≥ 1090/1310 mg/kg bw/day (6000 ppm): depression and ataxia,↑ rel liver wt, stippled appearance of liver, liver hypertrophy ≥ 1860/2090 mg/kg bw/day (9500 ppm): liver enlargement, liver w/granulomatous lesion 4030/2590 mg/kg bw/day (15000 ppm): mortality and ↓BW, bladder w/granulomatous lesions
4-week dietary toxicity CD-1 mouse PMRA 1711136	**NOAEL = 290 mg/kg bw/day (1900 ppm)** ≥900 mg/kg bw/day (6000 ppm): granulomatous lesions surrounding crystal deposits in the urinary bladder and occasionally in liver parenchyma, myocardium, diaphragmatic muscle and skeletal muscle, ↑ liver wt, pale and mottled appearance in liver, hepatocyte swelling, histopathological changes in the spleen and testes

Study/Species/ PMRA #	Results/Effects
	≥1400 mg/kg bw/day (9500 ppm): ↑ mortality, clinical signs of toxicity, ↓ BWG and FC, Leydig cell hyperplasia (slight), swelling & vacuolization 2300 mg/kg bw/day (15000 ppm): partial or total arrest of spermatogenesis at the spermatocyte 2 stage, Leydig cell hypertrophy
13-week dietary toxicity CD-1 mouse PMRA 1611930	**LOAEL = 260/330 mg/kg bw/day (1500 ppm)** ≥260/330 mg/kg bw/day (1500 ppm): centrilobular hepatocyte enlargement (♂); ↑ adrenal and liver wt (♀) ≥660 mg/kg bw/day (3000 ppm): adrenal zona fasciculata vacuolation (♀) ≥1100/1300 mg/kg bw/day (6000 ppm): crystalline deposits with associated multinucleated cells in a number of tissues, particularly in the urinary bladder (♂); ↑ extramedullary hematopoiesis, uterine atrophy and absence of corpora lutea (♀) 2100/2600 mg/kg bw/day (12000 ppm): mortality, clinical signs of toxicity, BW loss, ↓ FC.
13-week dietary toxicity SD rat PMRA 1611930	**NOAEL = 78/89 mg/kg bw/day (1000 ppm)** ≥151/189 mg/kg bw/day (2000 ppm): ↓ BW, ↓ BWG, ↓ FE, vacuolation of the adrenal zona fasciculata, enlarged cells of the adrenal zona glomerulosa; ↓ FC (♂); ↑ uterine atrophy, ↓ corpora lutea and ↓ ovarian wt (♀) ≥252/266 mg/kg bw/day (3000 ppm): ↓ FC, clinical signs (hunched posture, piloerection, emaciation); prostate and seminal vesicle atrophy, Leydig cell hyperplasia, reduced seminal vesicle secretion (♂); ↓ rel adrenal and pituitary wt, ↓ uterine wt, ↓ abs brain wt (♀) 355/408 mg/kg bw/day (5000 ppm): group was terminated during week 8 due to excessive toxicity: progressively ↓ FC, ↓ BW, weight loss and death (1), absent or abnormal spermatozoa (♂); Animals had abnormalities in liver, adrenals, uterus, ovaries, prostate, and seminal vesicles
13-week dietary toxicity CD/CRJ Rat PMRA 1711135	**NOAEL = 21/24 mg/kg bw/day (300 ppm)** ≥70/82 mg/kg bw/day (1000 ppm): swelling of the zona glomerulosa in the adrenal glands; ↓ BW (♂) 210/240 mg/kg bw/day (3000 ppm): clinical signs of toxicity (piloerection, rough fur), ↓ FC and WC, ↓ BW, ↓ wt of liver, spleen, thymus, kidneys and heart. Microscopic findings were observed in the liver, spleen and thymus
13-week dietary toxicity SD rat PMRA 1711117	**NOAEL = 15/18 mg/kg bw/day (250 ppm)** ≥15/18 mg/kg bw/day (250 ppm): ↓ abs pituitary wt (♀) (non-adverse) ≥31/36 mg/kg bw/day (500 ppm): ↑ adrenal wt, ↓ abs testes wt, ↓ prostate wt, adrenal zona fasciculata hypertrophy (♂) ≥49/59 mg/kg bw/day (800 ppm): ↓ BW, ↓ BWG, ↑ cellular vacuolation of adrenal zona fasciculata and glomerulosa; ↑ rel adrenal wt, ↓ abs thyroid wt (♀) 183/229 mg/kg bw/day (3000 ppm): ↑ rel liver wt, ↑ pale adrenals; macroscopically small prostate (1), slight/mild atrophy of seminiferous tubules, hyposecretion of prostate gland

Study/Species/ PMRA #	Results/Effects
	(♂); ↓ abs uterine wt (♀)
5-month dietary toxicity COBS rat PMRA 1220398	**NOAEL = 7.5 mg/kg bw/day (150 ppm)** ≥25 mg/kg bw/day (500 ppm): ↓BW, ↓ BWG
13-week dietary toxicity Beagle dog PMRA 1220399	**270 mg/kg bw/day (7200 ppm)**:↑ ALT, AST and ALP at 1-2 months; ↓ RBC, Hct and Hb in 1 ♂ at 2-3 months, 1 ♀ at 2 months. Hypogonadism (1 ♂), enlarged uterus (1 ♀) **Supplemental (small group size).** Results were highly variable due to low animal numbers
52-week dietary toxicity Beagle dog PMRA 1711121, 1711139, 1711141	**LOAEL = 4.1/4.3 mg/kg bw/day (100 ppm)** ≥4.1/4.3 mg/kg bw/day (100 ppm): ↑ adrenal wt; ↓ prostate wt (♂); ↓ ovary wt (♀) ≥24.92/28.25 mg/kg bw/day (600 ppm): transient ↑ erythrocytes with Heinz bodies (up to week 14), adrenal cortex with pallid zona glomerulosa due to fatty vacuolation (♂); slight retinal hyperreflection, lipofuscinosis in proximal convoluted tubular epithelium of kidneys (♀) 145.3/152.5 mg/kg bw/day (3600 ppm): ↑ ALP, ↑ liver wt,↓ RBC, Hb and Hct, ↑ Heinz bodies, platelet count and thromboplastin time, ↑ pigmented microphage agglomerates, vacuolation and pallid appearance of adrenal cortex (zonas fasciculata and glomerulosa) , submucosal granulomas and giant cells containing crystals in the urinary bladder, centriacinar hepatic cord atrophy, slight retinal hyperreflection; transient ↑ in ALT early in the study and in LDH late in the study, ↑ total bilirubin and albumin, ↑ heart wt (♀)
52-week dietary toxicity Beagle dog PMRA 1160497	**LOAEL = 7.8 mg/kg bw/day (200 ppm)** (♂) **NOAEL = 18.4 mg/kg bw/day** (♀) ≥7.8 mg/kg bw/day (200 ppm): ↓ prostate wt, ↑ adrenal wt (♂) 24.6/26.4 mg/kg bw/day (600 ppm): ↓ rel kidney wt, ↑adrenal wt; ↓RBC, Hct and Hb at weeks 4-36
3-week dermal toxicity NZW rabbit PMRA 1128945	**NOAEL = 1000 mg/kg bw/day** No treatment-related effects on mortality, food consumption, body weight, clinical behaviour, hematology, clinical chemistry, organ weights, gross pathology and histopathology
Chronic Toxicity/Oncogenicity Studies	
Chronic toxicity/ oncogenicity (dietary) CD-1 mouse PMRA 1147791,	**NOAEL =23/27 mg/kg bw /day (150 ppm)** ≥115/138 mg/kg bw/day (800 ppm): centrilobular hepatocyte enlargement; accentuated liver lobular markings (interim only), ↑ incidence of liver masses; generalized vacuolization and hypertrophy of testicular interstitial cells, ↑ non-glandular stomach hyperkeratosis (♂); amyloidosis in kidney (♀)

Study/Species/ PMRA #	Results/Effects
1147792 and 1147788	604/793 mg/kg bw/day (4000 ppm): ↓ BWG and BW, ↑ adrenal wt (int), ↑ ALT and AST, ↑ liver wt , enlargement of eosinophilic and fat containing hepatocytes; centrilobular hepatocyte vacuolization, ↑ thyroid wt (predominantly ♂), pigmented liver macrophages, ↑ testicular masses, flaccid and small testes (♂); hypertrophy of adrenal zona fasciculata cells (interim only), luteinization of interstitial cells of the ovaries, prominent granulosa cells, ↓ uterine and ovary wt, absence of corpora lutea, ↓ in endometrial hyperplasia, ↓ thickness of uterus epithelium, cortical scarring, ↑ spleen hemosiderosis and kidney wt (♀) **Neoplastic effects:** ↑ in benign and malignant liver tumours (14, 12, 20 and 52% in ♂ and 4, 4, 4, and 42% in ♀ at the control, low, medium and high dose groups; historical controls are 12-21% in ♂ and 0-2% in ♀); ↑ incidence of ovary luteomas (0, 4, 2 and 10% in control, low, medium and high doses; historical control is 0-8%) (♀)
Oncogenicity (dietary) Swiss albino (Hsd: Ola-MF1) mouse PMRA 2420938	**NOAEL = 23/26 mg/kg bw/day (150 ppm)** ≥117/132 mg/kg bw/day (750 ppm): ↑cholesterol, ↓AST, hepatocellular hypertrophy, adrenal cortical cell hypertrophy (interim only), absent cytoplasmic vacuolation of the kidneys; ↓ kidney wt, ↓epididymis wt, splenic hemosiderosis, Leydig cell hyperplasia (♂); ↓uterus wt (interim only), uterine epithelial hyperplasia (♀) 562/634 mg/kg bw/day (3500 ppm): ↓BW, ↓BWG, ↑liver wt, hepatic pathology (clear cell or eosinophilic focus, necrosis, multi-nucleated hepatocytes, pigmented macrophages, erythrophagocytosis), extramedullary hematopoiesis, ↑pigmentation of nose and cecum, dilated/cystic glands of stomach, vacuolar changes of the pancreas; ↑testes wt (interim only), adrenal cortical cell vacuolation and pigmented foamy macrophages (interim only), epithelial degeneration of the epididymis, cystic prostate, hyperplasia of mesenteric lymph nodes (♂); ↓brain wt, splenic hemosiderosis, mammary gland atrophy, ovarian cysts, ovarian atrophy, salivary gland atrophy (♀) **Neoplastic effects:** ↑ incidence of hepatocellular adenoma in ♂ and ♀ at the high dose; no ↑ in hepatocellular carcinoma. Combined Liver tumour incidence: ♂: 2/50, 0/50, 4/50, 13/50 ♀: 0/50, 1/50, 0/50, 6/50 Note: lacking histopathology of the prostate, epididymis and mammary gland in all animals of the low and mid-dose group
Oncogenicity/ chronic toxicity (dietary) Wistar rat PMRA 2420940	**NOAEL = 3.6/18 mg/kg bw/day (75/300 ppm)** ≥15 mg/kg bw/day (300 ppm): ↑ adrenal wt, ↑testes wt, cortical vacuolation of the zona fasciculata of the adrenal gland (♂) 75/93 mg/kg bw/day (1600 ppm): : marginal ↓BW and BWG, eosinophilic inclusions in the olfactory epithelium; ↑thymus wt, Leydig cell hyperplasia (♂) **Neoplastic effects:** ↑ incidence of Leydig cell tumours in the testes of high-dose ♂, ↑ incidence of uterine adenocarcinomas in high-dose ♀ Leydig cell tumour incidence ♂: 0/60, 1/60, 1/60, 14/60 Uterine adenocarcinoma incidence: ♀: 1/60, 1/21, 6/30, 5/60

Study/Species/ PMRA #	Results/Effects
	Note: lacking histopathology of the uterus and ovaries in all animals of the low and mid-dose group
Oncogenicity/ chronic toxicity (dietary) SD rat PMRA 1147789, 1147790, 1147787	**NOAEL = 6.1/8.4 mg/kg bw/day (150 ppm)** ≥12.4/16.5 mg/kg bw/day (300 ppm): ↑ centrilobular hepatocyte enlargement (interim), slight enlargement of adrenal zona glomerulosa cells, vacuolization in the zona fasciculata; ↑ in number and severity of kidney basophilic dilated cortical tubules containing eosinophilic colloid, ↑ liver wt, vacuolization of the adrenal zona reticularis, prostatic atrophy, ↓ epididymal spermatozoa and ↓ secretion in the seminal vesicles (♂); ↑ splenic hemosiderosis, ↑ in polypoid masses and uteri thickening (♀) 69/95 mg/kg bw/day (1600 ppm): ↓ BW and BWG. FC was slightly ↓. Rarefaction ↑ in lung petachiae; ↑ thyroid wt, atrophy of the seminiferous tubules, ↑ testicular interstitial cell hyperplasia, ↑ testes w/ epididymides wt and absence of epididymal spermatozoa (♂);↑ liver weights, enlargement of the adrenal zona glomerulosa, ↑ luminal dilation of the uterus, ↑ uterine fluid swelling/distension or cystic lesions (interim), ↑ dilated uterine endometrial glands, ↑ ovary wt, ovary tubular hyperplasia; ↑ incidence of extramedullary hematopoiesis and splenic hemosiderosis (interim) (♀) **Neoplastic effects:** ↑ incidence of testicular interstitial cell tumours Interstitial cell tumour incidence: 3/60, 7/60, 7/60, 29/60
Reproductive and Developmental Toxicity Studies	
Developmental toxicity (gavage) SD rat PMRA 1220403	≥100 mg/kg bw/day: ↓ maternal BW and BWG 200 mg/kg bw/day: ↑ incidence in late resorptions 400 mg/kg bw/day: ↓ FC, ↓ live fetuses, ↓ implantations **Supplemental**
Developmental toxicity (gavage) SD rat PMRA 1611940	**Maternal:** **NOAEL ≥ 200 mg/kg bw/day** No maternal toxicity was observed **Developmental:** **NOAEL = 90 mg/kg bw/day** 200 mg/kg bw/day: ↑ incidence of space between body wall and organs, ↑ incidence of small fetuses, ↓ fetal BW
Developmental toxicity (gavage) SD rat PMRA 1191364	**Maternal:** **NOAEL = 20 mg/kg bw/day** ≥120 mg/kg bw/day: ↓BWG, ↓ FC and FE, stained fur, enlarged adrenals 250 mg/kg bw/day: 9/25 dams died or were killed in extremis (clinical signs included prostration, ↓ motor activity, facial and urogenital staining) **Developmental:**

Study/Species/ PMRA #	Results/Effects
	NOAEL = 20 mg/kg bw/day ≥120 mg/kg bw/day: ↓ anogenital distance in ♂ fetuses, ↑ in runts in both sexes 250 mg/kg bw/day:↓ fetal BW and ↑ in edema in both sexes
Developmental toxicity (gavage) NZW rabbit PMRA 1220404	**Maternal**: **LOAEL = 100 mg/kg bw/day** ≥100 mg/kg bw/day: ↓ BWG, ↓ FC ≥200 mg/kg bw/day: ↑ incidence of total resorptions 400 mg/kg bw/day: 9/17 dams died, all between days 20-27, only 1 dam carried pregnancy to term, weight loss ↓ total # of implantation sites **Developmental:** **NOAEL = 100 mg/kg bw/day** ≥200 mg/kg bw/day: ↓ fetal wt 400 mg/kg bw/day: possible teratogenic effects (4/6 surviving fetuses had missing rib)
Developmental toxicity (gavage) NZW rabbit PMRA 1208829, 1209635	**Maternal:** **NOAEL= 20 mg/kg bw/day** 60 mg/kg bw/day: ↓ BWG 200 mg/kg bw/day: ↓ BW and BW loss, clinical signs (hair loss, diarrhoea, ↓ urination and defecation). 10/18 does delivered litters, two of which had totally resorbed litters. ↑ early abortions and ↓ in viable fetuses **Developmental:** **NOAEL = 60 mg/kg bw/day** 200 mg/kg bw/day: ↑ presacral vertebra
Range-finding developmental toxicity (gavage) CD rat PMRA 1208830	≥120 mg/kg bw/day: clinical signs (flaccid muscles, lack of spatial awareness). ≥240 mg/kg bw/day: ↓BW, ↓ BWG ≥400 mg/kg bw/day: significant toxicity, 1/6 dams died, 1 viable litter, ↑ in clinical signs (prostration, flaccid muscles, ataxia, awareness, poor righting reflex, piloerection, pallor, ocular discharge, facial or urinogenital coat staining and vaginal bleeding), ↓ in litter size, small and large placenta, ↑ histopathological findings in fetuses, abnormal skeletal structure, retarded and incomplete ossification 800 mg/kg bw/day: 8/14 dams died, no viable litters **Supplemental**
2-generation (2-litter) reproductive toxicity (dietary)	**Parental:** **NOAEL = 21 mg/kg bw/day (300 ppm)** ≥55/71 mg/kg bw/day (1000 ppm): ↓FC; ↓BW, BWG (pre-mating)(F_0 F_1)

Study/Species/ PMRA #	Results/Effects
CD rat PMRA 1166135 1166136	190 mg/kg bw/day (3000 ppm*): ↓BWG (gestation)(F_1) **Reproductive:** **NOAEL = 71 mg/kg bw/day (1000 ppm)** 190 mg/kg bw/day (3000 ppm*): ↓ birth weight, ↓ number of pups delivered, (F_{1a}, F_{1b}, F_{2a}, F_{2b})↓ pup live birth index (F_{1a}, F_{1b}), ↓ live litter sizes, (partially due to still births) (F_{2a}, F_{2b}) **Offspring:** **NOAEL = 71 mg/kg bw/day (1000 ppm)** 190 mg/kg bw/day (3000 ppm): ↑ incidence in clinical signs in pups (smallness, reduced mobility, unkempt appearance, brown material around eyes and nasal area, hunching and/or tremors) (F_{1a}, F_{1b}), ↓ pup viability index, ↓ weaning index, (F_{1a}, F_{1b}), ↓ pup BW (F_{2a}, F_{2b}) *3000 ppm was reduced to 2000 ppm at time of first F_{1a} mating due to excessive toxicity
3-generation (1-litter) reproductive toxicity (dietary) SD rat PMRA 1220402	100 mg/kg bw/day (1000 ppm for 5 wks, 2000 ppm for 8 weeks): F_o: mean # of live pups at day 4↓ F_1: ↓ BW in ♀ weeks 9-13, mean # of live pups at day 4↓ F_2: ↓ BW at start of post-weaning period in both sexes. ♂ caught up in weight by week 13, whereas ♀ did not and had ↓ BWG weeks 9-13 F_3: no treatment-related effects **Supplemental**
Genotoxicity Studies	
Gene mutation S. typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538. PMRA 1711146	Negative with metabolic activation (10 - 5000 µg/plate) and without metabolic activation (1 - 250 µg/plate)
Gene mutation (i) S. typhimurium TA98, TA100, TA1535, TA1537, TA1538 (ii) E.coli K12, GY5057 (iii) E.coli W3110 (pol A), p3478 (pol A) (iv) S. cerevisiae D7 PMRA 1711143	Negative in all with and without metabolic activation at (i) 25-200 µg/plate (ii) 0.05-1000 µg/ml (iii) 12.5-200 µg/plate (iv) 62.5-500 µg/ml

Study/Species/ PMRA #	Results/Effects
Gene mutation (i) S. typhimurium TA98, TA100, TA1535, TA1537 (ii) S. cerevisiae D7 strain PMRA 1711145	Negative at (i) 12.5 - 250 µg/ml without activation; spot test at 1000 µg/plate; 1 - 1000 µg/plate with activation (ii) 250 µg/ml without metabolic activation **Supplemental**
HGPRT mutation Chinese hamster ovary cells PMRA 1216614	Negative with metabolic activation (100 - 1500 µg/ml) and without metabolic ctivation (5 - 100 µg/ml)
Chromosomal aberration Chinese hamster ovary cells PMRA 1216612	Negative with metabolic activation (40 - 400 µg/ml) and without metabolic activation (15 - 150 µg/ml)
Sister chromatid exchange Chinese hamster ovary cells PMRA 1711147	Negative with metabolic activation (5 - 400 µg/ml) and without metabolic activation (5 - 100 µg/ml). .
Micronucleus (gavage) CD-1 mice PMRA 1166140	3000 mg/kg bw: no significant ↑ in micronuclei. 1/20 ♂ and 8/20 ♀ died, indicating a dose above MTD. The animals had corresponding bone marrow depression Note: In the range-finding phase of the study 4000 mg/kg bw was lethal to 3/4♂ mice; no mortality was seen at 3000 mg/kg bw **Negative**
Metabolite/Mechanistic Studies	
Testosterone secretion in vitro Porcine cultured Leydig cells PMRA 1166141	Iprodione and two of its metabolites (RP 36112 and RP 36115) inhibited hCG-stimulated testosterone secretion at 1 µg/ml to a maximal (≈ 80%) inhibition at 3-10 µg/ml. Inhibition was observed within 3 hrs of exposure. This effect was fully reversible after cells were transferred into iprodione-free media for 72 hours
Testosterone secretion in vitro Immature porcine Leydig cells	Iprodione (10 µg/ml) had no effect on hCG-stimulated cAMP production. However, iprodione, RP36112 and RP 36115 competitively inhibited steroidogenesis in cultured Leydig cells. Incubation of cells with 22ROHCT (a cholesterol substrate that passes through mitochondrial membranes without the need for active transport) caused the inhibitory effect of iprodione and RP36115 to disappear, suggesting that these compounds prevent the active

Study/Species/ PMRA #	Results/Effects
PMRA 1171335	transport and availability of cholesterol for the cholesterol side chain cleavage enzyme in Leydig cells. RP36112 appears to act downstream from the cholesterol step by modulating steroidogenic enzyme activity
Endocrine toxicity 2 week study (diet) SD rat testicular sections from treated and untreated animals PMRA 1171336	175 mg/kg bw/day (3000 ppm): significant ↑ plasma LH levels (suggesting a rapid compensatory mechanism to correct any effect on steroidogenesis), ↓BW, ↓BWG, ↓FC, ↑ adrenal and testes wts and ↓ total accessory sex organ, epididymal and kidney wts in vivo exposure had no effect on secretion of testosterone from testicular sections incubated in vitro either with or without hCG stimulation in vitro incubation of testicular slices from untreated controls with iprodione (1 – 100 µg/ml for 1 hour) caused a dose-dependent ↓in testosterone secretion, regardless of hCG stimulation. Although the inhibition was dose-related, there may have been a response plateau reached around 10-100 µg/ml
Endocrine toxicity 2-week range-finding study, 4-week main study (gavage) SD rat in vitro binding to rat prostatic androgen receptors PMRA 1166142 1171296	**Range-finding study:** ≥300 mg/kg bw/day: ↓BW, ↑ FSH (< than flutamide) 600 mg/kg bw/day: ↓ FC, ↑ liver wt, ↓ abs testes wt, epididymes wt, all accessory sex organs, prostate and seminal vesicles (< than flutamide), ↑ LH (< than flutamide) **Main study:** 600 mg/kg bw/day: mortality (3/18 died), BW loss after 7 days, ↓ BWG days 8-23, ↓ FC. ↑LH and FSH concentrations after 15 days (but not after 30 days). At necropsy testosterone concentrations were comparable between treated and control rats. ↑ Estradiol concentrations, ↑ liver and adrenal wts, ↓ epididymides wt, ↓ all accessory sex organs wt, ↓prostate wt and ↓ seminal vesicles wt (to lesser extent than after flutamide). ↑ Incidence of glandular atrophy of the seminal vesicles and prostate gland (incidence similar to pair-fed, but of greater severity). ↑ Incidence of cytoplasmic vacuolation within adrenal *zona fasciculata* and centrilobular hepatocellular hypertrophy (> than flutamide). Subtle changes in the secretion pattern of testosterone and LH were noted **In vitro study:** Iprodione and most of its metabolites had relative binding affinities of <0.001% to the androgen receptor, whereas RP 25040, RP 36112 and RP 36115 had appreciable binding (= 0.006, 0.0028 and 0.0012%, respectively). Flutamide binding =0.01%, testosterone = 35%, and dihydrotestosterone = 100%. Therefore, iprodione does not have high affinity for the androgen receptor and there is little evidence for competitive binding or inhibition
Endocrine toxicity 2, 7 or 14 day study (diet) SD ♂rat PMRA 1171296	150 mg/kg bw/day: ↓ BW, ↓ BWG, ↓ FC, ↑ rel liver, testes and adrenal wt, ↓ rel total accessory sex organ wts. No effect on epididymal wt No significant differences in testosterone (from plasma or testicular homogenate) 1 hour after hCG challenge
Endocrine toxicity ~3 week study	≥50 mg/kg bw/day: ↓ serum testosterone, ↑ BW at preputial separation initiation, ↑ adrenal wt

Study/Species/ PMRA #	Results/Effects
(gavage) SD ♂ rat (PND 23-53) PMRA 1700055	≥100 mg/kg bw/day: delayed initiation and completion of preputial separation 200 mg/kg bw/day: ↑ liver wt, ↓ androgen-dependent seminal vesicle and epididymides wt
Hormone measurements in single-dose study (gavage) SD rat PMRA 2002756	≥70 mg/kg bw: testosterone levels (2hrs post dose), ↑ LH levels (4hrs post dose)
Quantification of iprodione and metabolites in single-dose study (gavage) SD ♂ rat PMRA 1611929	70 mg/kg bw: Mean whole blood radioactivity concentration 5.0-14 µg equiv./g, between 0.5 – 10 hrs post dose Mean testes total radioactivity concentration 5.5-10 µg equiv./g, between 0.5 – 10 hrs post dose Mean testes iprodione parent compound fraction radioactivity concentration 0.95 - 8.9 µg equiv./g, between 0.5 – 10 hrs post dose
Hormone measurements in single-dose study (gavage) SD Rats PMRA 1611927	70 mg/kg bw: ↓ testosterone levels 0.5hrs post dose with a peak at 2hrs post dose; ↑ LH levels 2 and 4hrs post dose in each dose 300 mg/kg bw: ↓ testosterone levels 0.5hrs post dose with a peak at 1hr post dose and significant ↓ still occurring at 4hrs
Leydig cell proliferation in 14 day study (gavage) SD Rats PMRA 1611915	6 mg/kg bw/day: ↑ proliferation index (14%) (non-significant change) 70 mg/kg bw/day: ↑ proliferation index (30%). One animal with soiled fur around nose, nasal discharge, noisy respiration, increased salivation, reduced motor activity, ↓ BWG 300 mg/kg bw/day: ↑ proliferation index (74%), soiled anogenital fur
Hormone measurements in 14 day study (gavage) SD Rats PMRA 1611936	6 mg/kg bw/day: ↓ testosterone levels 1 hr post dose (non-significant change) 70 mg/kg bw/day: ↓ testosterone levels (2hrs post dose), ↑ LH levels (4hrs post dose) 300 mg/kg bw/day: ↓ testosterone levels (1, 2 and 4 hrs post dose), ↑ LH levels (4hrs post dose), soiled anogenital fur, ↓ FC, ↓ BWG
Liver enzyme induction in 7 and	696 mg/kg bw/day (8000 ppm): liver cell proliferation and ↑ liver wt on days 8 and 15 and centrilobular hypertrophy on day 15. Dose-dependent ↑ microsomal enzyme activities (CYP

Study/Species/ PMRA #	Results/Effects
14-day study (diet) CD-1 mouse PMRA # [illegible]	[illegible] and total cytochrome P-450, ↑ ALT levels, ↑ [illegible] and pentoxycoumarin, ↓ bilirubin ≥1150 mg/kg bw/day (10000 ppm): centrilobular hypertrophy on days [illegible], ↑ plasma protein, albumin, cholesterol, AST, ALP

Table 3 Metabolite Identification

RP [illegible]	(Dichloro-3,5 phenyl)-3 hydantoine
RP 30228	(N dichloro-3,5 phenylcarbamoyl)-1 isopropyl-3 hydantoine
RP 32490	Carbamoyl-1 (dichloro-3,5 phenyl)-3 hydantoine
RP 36112	(Dichloro-3,5 phenyl) Carbamoyl-1 hydantoine
RP [illegible]	(Dichloro-3,5 hydroxy-4 phenyl)-1 Biuret
RP [illegible]	(Dichloro-3,5 phenyl)-1 Biuret
RP 36116	(Dichloro-3,5 phenyl) Carbamoyl-1 (carboxy-1 ethyl)-3 hydantoine
RP [illegible]	(Carboxy-1 ethyl) Carbamoyl-1 (dichloro-3,5 phenyl)-3 hydantoine
RP 36119	(Dichloro-3,5 hydroxy-4 phenyl)-3 Carbamoyl-1 isopropyl-3 hydantoine

Appendix IV Dietary Food and Drinking Water Exposure and Risk Estimates for Iprodione

Acute Food Only Exposure and Risk Assessment

Population Group	Exposure from Food[1]	
	mg/kg bw	%ARfD[2]
Females (13-49 yrs)	0.0069	10

ARfD = Acute Reference Dose
[1] 99.9th percentile of exposure
[2] ARfD = 0.07 mg/kg bw, based on NOAEL of 20 mg/kg bw and composite assessment factor of 300

Chronic Food Only Exposure and Risk Assessment

Population Group	Exposure from Food	
	mg/kg bw/day	%ADI[1]
General Population	0.00016	1
All Infants (<1 years)	0.00019	1
Children 1-2 years	0.00054	4
Children 3-5 years	0.00039	3
Children 6-12 years	0.00023	<1
Youth 13-19 years	0.00013	<1
Adults 20-49 years	0.00011	<1
Adults 50+ years	0.00011	<1
Females 13-49 years	0.00012	<1

ADI = Acceptable Daily Intake
[1] ADI = 0.014 mg/kg bw/day, based on NOAEL of 4.1 mg/kg bw/day and composite assessment factor of 300

Cancer Food Only Exposure and Risk Assessment

Population Group	Lifetime Cancer Risk[1]
General Population	1×10^{-6}

[1] Cancer Risk Unit = q_1^* (0.0439 (mg/kg bw/day)$^{-1}$) × chronic exposure

Acute Food and Drinking Water Exposure and Risk

Population Group	Acute Food and Drinking Water Exposure[1]					
	Turf Use		Orchard Use		Canola Use	
	mg/kg bw	%ARfD[2]	mg/kg bw	% ARfD[2]	mg/kg bw	% ARfD[2]
Females 13-49 years	0.035	52	0.007	11	0.007	11

ARfD = Acute Reference Dose
[1] 99.9th percentile of exposure
[2] ARfD = 0.07 mg/kg, based on NOAEL of 20 mg/kg bw and composite assessment factor of 300

Chronic Food and Drinking Water Exposure and Risk

Population Group	Chronic Food and Drinking Water Exposure					
	Turf Use		Orchard Use		Canola Use	
	mg/kg bw/d	%ADI[1]	mg/kg bw/d	% ADI[1]	mg/kg bw/d	% ADI[1]
General Population	0.0054	39	0.0005	4	0.0004	3
All Infants (<1 years)	0.0176	126	0.0017	12	0.0011	8
Children 1-2 years	0.0083	60	0.0009	7	0.0008	6
Children 3-5 years	0.0077	55	0.0008	6	0.0007	5
Children 6-12 years	0.0053	38	0.0005	4	0.0004	3
Youth 13-19 years	0.0039	28	0.0004	3	0.0003	2
Adults 20-49 years	0.0050	36	0.0005	3	0.0003	2
Adults 50+ years	0.0053	38	0.0005	4	0.0003	2
Females 13-49 years	0.0050	56	0.0005	3	0.0003	2

ADI = Acceptable Daily Intake, d = day

[1] ADI = 0.014 mg/kg bw/day, based on NOAEL of 4.1 mg/kg bw/day and composite assessment factor of 300

Cancer Food and Drinking Water Exposure and Risk

Population Group	Lifetime Cancer Risk Unit[1]		
	Turf Use[2]	Orchard Use[2]	Canola Use[2]
General Population	4×10^{-7}	5×10^{-8}	3×10^{-8}

[1] Cancer Risk Unit = q1* [0.00009 (mg/kg bw/day)$^{-1}$] × chronic exposure

Appendix V Food Residue Chemistry Summary

Iprodione is a contact fungicide registered for use on a variety of crops in Canada including alfalfa, beans, cabbage, canola, cauliflower, cucumbers, garlic, ginseng, grapes, leeks, lettuce, onions, raspberries, stone fruits (apricot, cherry, peach, plum/prune), strawberries, and tomatoes. It is also registered for use on non-food crops including ornamentals, conifer seedlings, and turf.

The nature of the residue in plants and animals is understood. In plants treated with foliar applications, iprodione equivalent residues remained fairly immobile and were primarily localized in the stems and leaves. The only significant metabolite identified in edible portions of plants was the isomer RP30228 found in treated rice grain. The established residue definition in plants is iprodione, RP32490, and RP30228. Given that iprodione was the predominant compound found in plants, it is proposed that the residue definition for the purposes of enforcement be revised to iprodione only. For the risk assessment, the residue definition should include iprodione in all plant crops except cereal grains, where the residue definition is iprodione and RP30228. In animals, iprodione was shown to be extensively metabolized. The metabolic profile was similar in all animals tested (rat, cow, goat, and hens). The major metabolites identified were RP36114 in milk and RP32490 in eggs, milk, and tissues. The current residue definition established in animals includes iprodione, the isomer RP30228, and the metabolite RP32490. Based on the available data, the residue definition for the risk assessment and enforcement should remain the same in all animal matrices except milk where an additional metabolite, RP36114 was found in significant amounts. Thus, the proposed residue definition for milk is iprodione, RP32490, RP30228, and RP36114.

Gas chromatography (GC), gas liquid chromatography (GLC), and high performance liquid chromatography (HPLC) methods have been developed to analyze for iprodione, and/or its metabolites RP30228, RP32490, and RP36114 in plant and animal matrices for the purposes of residue data collection. The HPLC-MS method has been validated in independent laboratories and is suitable for use as an enforcement method.

Magnitude of residue data on file were adequate for most registered uses. However, additional data are required to establish or revise MRLs on greenhouse cucumbers, garlic, cauliflower, cabbage, and greenhouse tomatoes. There were either inadequate residue data to determine the magnitude of residue on these commodities or there were limited residue data which indicated that iprodione may potentially exceed the MRL.

There were adequate feeding studies available for cows and poultry. Based on the residue data in the feeding studies and the maximum theoretical dietary burden, the highest anticipated residues in animals were determined to range from 0.0001 ppm in ruminant muscle to 0.002 ppm in poultry liver. Given the low anticipated residues, exposure from animals is expected to negligible and animal commodities were not included in the dietary assessment. There are currently no MRLs specified for animal commodities in Canada; there are sufficient residue data to establish MRL for animal matrices at the HPLC-MS method LOQ at 0.50 ppm for animal tissues, 0.25 ppm for eggs, and 0.07 ppm for milk in support of potential imports from the United States.

Crop rotation trials on file indicate that iprodione and metabolite residues may potentially accumulate in rotational crops. As there are currently no plant back interval (PBI) restrictions specified on labels, it is proposed that a PBI of 30 days be specified for all crops except root vegetables (crop group 1) and leafy Brassica greens (crop group 5b). For crop group 1 and 5b the PBI should be 12 months.

No MRLs and PBI restrictions will be proposed at this time in consideration of the risk concerns identified from iprodione exposure in food and drinking water and the proposed decision to cancel all iprodione registrations in Canada.

Appendix VI Occupational Exposure Risk Estimates for Iprodione

Table 1 Wettable Powder Formulation: Occupational Exposure Risk Assessment Summary

Scenario		**Mixer/Loader/Applicator**	**Post-Application**[2]
USC	**Crop**		
5/6	Greenhouse Lettuce	Hand held equipment: Mid level PPE + respirator	REI: 0.5 days
	Greenhouse Cucumber	Hand held equipment: Mid level PPE + respirator	REI: not determined; data required
	Greenhouse Tomato	Hand held equipment: Mid level PPE + respirator	REI: not determined; data required
6/27	Conifer seedlings (spruce, fir, hemlock and cedar) - container or bareroot conifer seedlings in greenhouses and conifer nurseries	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	Greenhouse REI: 0.5 days Outdoor REI: 0.5 - 6 days
	Ornamentals[1]	Hand held equipment: Mid level PPE + respirator Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	Greenhouse Cut Flower REI: not determined; data required Outdoor Cut Flower REI: 0.5 – 65 days Greenhouse potted flower REI: 0.5 days Outdoor potted flower REI: 0.5-18 days
	Ornamentals -Celosia, Salvia	Soil Drench: Closed Mix/Load and Baseline PPE	Soil drench only; no foliar contact REI: 0.5 days
13	Alfalfa grown for seed (Saskatchewan, Alberta, Manitoba and the Peace River region of British Columbia)	Aerial and groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 - 2 days
7, 13, 14	Canola	Aerial and groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 days
14	Grapes	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 – 137 days
	Lettuce, field (head & leaf)	Groundboom: Baseline PPE	REI: 0.5 – 1 day
	Dry common beans (white and kidney)	Aerial and groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 - 2 days
	Ginseng	All equipment: Baseline PPE	REI: 0.5 days
	Snap beans	Aerial: Closed Mix/Load and Baseline PPE Groundboom: Baseline PPE	REI: 0.5- 2 days
	Raspberry	All equipment: Baseline PPE	REI: 0.5 - 6 days
	Strawberry	All equipment: Baseline PPE	REI: 0.5 days
	Plum/prune	All equipment: Baseline PPE	REI: 0.5 - 20 days
	Cherry (sweet)	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 - 20 days
	Peach	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 - 20 days
	Apricot	All equipment: Baseline PPE	REI: 0.5 - 20 days
	Cauliflower	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE + respirator	REI: 7 - 26 days
	Cabbage (stored)	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE + respirator	REI: 7 - 26 days
	Onion (dry bulb)	Groundboom: Baseline PPE	REI: 0.5 - 14 days

Scenario		Mixer/Loader/Applicator	Post-Application[2]
USC	Crop		
	Leek	Groundboom: Baseline PPE	REI: 0.5 - 14 days
30	Turf – fairways, putting greens and other turf areas including sod production consisting of Kentucky bluegrass, bentgrass, perennial ryegrass and fine fescue, or where these mixtures predominate (excluding residential turf)	Groundboom: Closed Mix/Load and Baseline PPE Hand held equipment: Baseline PPE + respirator	REI: 0.5 -2 days

[1] These include the following ornamentals: *Adiantum* spp., *Aphelandra squarrosa, Aralia elegantissima, Aralia sieboldii, Asparagus sprengeri, Asparagus plumosus, Azalea* spp., *Begonia rex* var. Fireglow, *Chrysanthemum* spp. (all year round), *Chlorophytum* spp., *Cineraria* spp., *Cissus antarctica, Croton* spp var. Bravo, *Cyclamen* spp., *Dracaena* spp var. Rededge, *Episcia cupreata, Euonymus* spp., *Euphorbia splendens, Ficus* spp., *Fittonia* spp., *Fuchsia* spp., *Geranium* (Zonal), *Gesneria* spp., *Gynura sarmentosa, Hedera* spp., *Hypoestes sanguinolenta, Impatiens* spp., *Iresine herbstii, Kalanchoe* spp., *Maranta* spp., *Monstera deliciosa* 'borsigiana', *Neanthe bella, Nepeta* spp. (ginger plant), *Nephrolepis* spp., *Pelargonium* spp., *Peperomia caperata, Peperomia hederifolia, Peperomia magnoliifolia, Philodendron scandens, Pilea cadierei, Poinsettia* spp., *Primula* spp., *Rhoicissus* spp., *Ruellia makoyana, Saintpaulia ionantha, Saxifraga stolonifera, Senecio macroglossus* 'variegatum', *Setcreasea purpurea, Sinningia* spp. (Gloxinia), *Solanum capsicastrum, Rosa hybrida* c.v. Samantha.

[2] REIs from individual tasks are grouped together.

Table 2 Wettable Granule Formulations: Occupational Exposure Risk Assessment Summary

Scenario		Mixer/Loader/Applicator	Post-Application[2]
USC	Crop		
5/6	Greenhouse Lettuce	Hand held equipment: Mid level PPE	REI: 0.5 days
	Greenhouse Cucumber	Hand held equipment: Mid level PPE	REI: not determined; data required
	Greenhouse Tomato	Hand held equipment: Mid level PPE	REI: not determined; data required
6/27	Conifer seedlings (spruce, fir, hemlock and cedar) - container or bareroot conifer seedlings in greenhouses and conifer nurseries	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	Greenhouse REI: 0.5 days Outdoor REI: 0.5 - 6 days
	Ornamentals[1]	Hand held equipment: Mid level PPE Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	Greenhouse Cut Flower REI: not determined; data required Outdoor Cut Flower REI:0.5 – 65 days Greenhouse potted flower REI: 0.5 days Outdoor potted flower REI: 0.5-18 days
	Ornamentals -Celosia, Salvia	Soil Drench: Baseline PPE	Soil drench only; no foliar contact REI: 0.5 days
13	Alfalfa grown for seed (Saskatchewan, Alberta, Manitoba and the Peace River region of British Columbia)	Aerial: Maximum PPE (M/L) Groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 - 2 days
7, 13, 14	Canola	Aerial: Maximum PPE (M/L) Groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 days
14	Grapes	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 – 137 days
	Lettuce, field (head & leaf)	Groundboom: Baseline PPE	REI: 0.5 – 1 day
	Dry common beans (white and kidney)	Aerial: Maximum PPE (M/L) Groundboom: Closed Mix/Load and Baseline PPE	REI: 0.5 - 2 days
	Ginseng	All equipment: Baseline PPE	REI: 0.5 days
	Snap beans	Aerial: Maximum PPE Groundboom: Baseline PPE	REI: 0.5- 2 days

Scenario		Mixer/Loader/Applicator	Post-Application[2]
USC	Crop		
	Raspberry	All equipment: Baseline PPE	REI: 0.5 - 6 days
	Strawberry	All equipment: Baseline PPE	REI: 0.5 days
	Plum/prune	All equipment: Baseline PPE	REI: 0.5 - 20 days
	Cherry (sweet)	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 - 20 days
	Peach	Airblast: Baseline PPE and CR hat Handheld equipment: Baseline PPE	REI: 0.5 - 20 days
	Apricot	All equipment: Baseline PPE	REI: 0.5 - 20 days
	Cauliflower	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	REI: 7 - 26 days
	Cabbage (stored)	Airblast: Baseline PPE and CR hat Groundboom: Baseline PPE	REI: 7 - 26 days
	Onion (dry bulb)	Groundboom: Baseline PPE	REI: 0.5 - 14 days
	Leek	Groundboom: Baseline PPE	REI: 0.5 - 14 days
30	Turf – fairways, putting greens and other turf areas including sod production consisting of Kentucky bluegrass, bentgrass, perennial ryegrass and fine fescue, or where these mixtures predominate (excluding residential turf)	Groundboom: Mid level PPE Hand held equipment: Baseline PPE + respirator	REI: 0.5 -2 days

[1] These include the following ornamentals: *Adiantum* spp., *Aphelandra squarrosa*, *Aralia elegantissima*, *Aralia sieboldii*, *Asparagus sprengeri*, *Asparagus plumosus*, *Azalea* spp., *Begonia rex* var. Fireglow, *Chrysanthemum* spp. (all year round), *Chlorophytum* spp., *Cineraria* spp., *Cissus antarctica*, *Croton* spp var. Bravo, *Cyclamen* spp., *Dracaena* spp var. Rededge, *Episcia cupreata*, *Euonymus* spp., *Euphorbia splendens*, *Ficus* spp., *Fittonia* spp., *Fuchsia* spp., *Geranium* (Zonal), *Gesneria* spp., *Gynura sarmentosa*, *Hedera* spp., *Hypoestes sanguinolenta*, *Impatiens* spp., *Iresine herbstii*, *Kalanchoe* spp., *Maranta* spp., *Monstera deliciosa* 'borsigiana', *Neanthe bella*, *Nepeta* spp. (ginger plant), *Nephrolepis* spp., *Pelargonium* spp., *Peperomia caperata*, *Peperomia hederifolia*, *Peperomia magnoliifolia*, *Philodendron scandens*, *Pilea cadierei*, *Poinsettia* spp., *Primula* spp., *Rhoicissus* spp., *Ruellia makoyana*, *Saintpaulia ionantha*, *Saxifraga stolonifera*, *Senecio macroglossus* 'variegatum', *Setcreasea purpurea*, *Sinningia* spp. (Gloxinia), *Solanum capsicastrum*, *Rosa hybrida* c.v. Samantha.

[2] REIs from individual tasks are grouped together.

Table 3 Suspension Formulation: Occupational Exposure Risk Assessment

Scenario		Mixer/Loader/Applicator	Post-Application[1]
USC	Crop		
13	Alfalfa grown for seed (Saskatchewan, Alberta, Manitoba and the Peace River region of British Columbia)	Aerial: Baseline PPE Groundboom: Mid level PPE	REI: 0.5 - 2 days
7, 13, 14	Canola	Aerial: Baseline PPE Groundboom: Mid level PPE	REI: 0.5 days
10	Canola commercial seed treatment	Closed mix/load/transfer, Mid Level PPE + respirator Planting: Baseline PPE	
	Canola on-farm seed treatnent	Open mix/load, Baseline PPE	
	Mustard	Closed mix/load/transfer, Mid Level PPE + respirator Planting: Baseline PPE	
	Garlic	Data required	
	Carrot	Planting: Baseline PPE	
10	Potato Seed Piece Treatment	Baseline PPE	
30	Turf – fairways, putting greens and other turf areas including sod production consisting of Kentucky bluegrass, bentgrass, perennial ryegrass and fine fescue, or where these mixtures predominate (excluding residential turf)	All equipment: Baseline PPE	REI: 0.5 -2 days

[1] REIs from individual tasks are grouped together

Table 4 Granular Formulation: Occupational Exposure Risk Assessment Summary

Scenario		Mixer/Loader/Applicator	Post-Application[1]
USC	Crop		
30	Turf – fairways, putting greens and other turf areas including sod production consisting of Kentucky bluegrass, bentgrass, perennial ryegrass and fine fescue, or where these mixtures predominate (excluding residential turf)	All equipment: Baseline PPE	REI: 0.5 -2 days

[1] REIs from individual tasks are grouped together

Appendix VII Supplemental Maximum Residue Limit Information (MRL) — International Situation and Trade Implications

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices. There are iprodione MRLs or tolerances established in Canada, the United States, and by CODEX Alimentarius. The MRLs and tolerances can be found in Table 1 and Table 2.

The MRLs for iprodione are proposed for revocation to reduce dietary risk and to align with the proposed decision to cancel all registered uses in Canada. This may cause trade conflicts between Canada and other countries. The PMRA will consult with all interested stakeholders before making a final decision on MRL changes.

Table 1 Comparison between MRLs in Canada and in Other Jurisdictions

Commodity	MRL or Tolerance (ppm)		
	Canada[1]	United States[2]	Codex[3]
Almond nuts	0.3	0.3 (nuts)	0.2
Animals except poultry	-	0.5 (fat, meat, byproducts except liver and kidney) 3 (kidney, liver)	-
Animal – poultry	-	5 (fat) 1 (liver, meat) 0.5 (byproducts except liver)	-
Apricots	3	20	-
Barley	-	-	2
Beans (dry and succulent)	2	2	0.1 (dry) 2 (common)
Blackberries	25	-	30
Blueberry	-	15	-
Boysenberry	-	15	
Broccoli	-	25	25
Cabbage	-	-	10
Carrot roots	5	5	-
Cauliflower	-	-	-
Cherries	5	-	20
Cranberry subgroup 13A	-	-	25
Cucumbers	0.5	-	2
Currant	-	15	-
Eggs	-	1.5	-
Garlic	-	0.1	-
Ginseng	4 (root)	2 (ginseng) 4 (dried root)	-
Grapes	10	60	10
Kiwifruit	0.5	10	5
Leaf and head lettuce	25	25	10 (head) 25 (leaf)
Leeks	13	-	-
Loganberries	25	-	-
Milk	-	0.5	-
Mustard greens	11	-	-
Mustard seed	-	15 (regional)	-
Nectarines	10	20 (postharvest)	-
Onion (dry bulb)	0.2	0.50.5	0.2
Peach	10	20 (postharvest)	10
Peanut	-	0.5	-
Plums/Prunes	2	20 (postharvest, prune)	

Commodity	MRL or Tolerance (ppm)		
	Canada[1]	United States[2]	Codex[3]
Pome fruits	-	-	5
Potato	-	0.5	-
Raisins	60	300	
Rapeseed (canola)	1	-	0.5
Raspberries	25	15	30
Rice	-	10 (grain)	10 (husked)
Spices, roots and rhizomes	-	-	0.1
Spices, Seeds	-	-	0.05
Strawberries	5	15	10
Sugar beet	-	-	0.1
Sunflower seed	-	-	0.5
Tomatoes	0.5	-	5
Underlinted cotton seeds	0.1	-	0.1
Wine	5	-	-
Witloof chicory (sprouts)	-	-	1

MRL and Tolerance information checked on June 5th, 2015

[1] By virtue of subsection B.15.002(1) of the Food and Drug Regulations, the MRL of foods for which MRLs have not specifically been established is 0.1 ppm.

[2] As per Title 40 Part 180.261 of the United States Code of Federal Regulations. United States tolerances for livestock feed items (alfalfa, almond hulls, field pea vines and field pea hay) are not presented.

[3] Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

Table 2 Current Residue Definition for MRLs in Canada and Other Jurisdictions

Jurisdiction	Residue Definition
Canada[1]	3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide, including the metabolites 3-isopropyl-*N*-(3,5-dichlorophenyl)-2,4-dioxoimidazolidine-1-carboxamide [RP30228] and 3-(3,5-dichlorophenyl)-2,4-dioxoimidazolidine-1-carboxamide [RP32490]
United States	Plants: Iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer 3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide, and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboxamide Animals: Iprodione [3-(3,5-dichlorophenyl)-*N*-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methylethyl)-*N*-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide, and its metabolites [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboxamide] and [*N*-(3,5-dichloro-4-hydroxyphenyl)-ureido-carboxamide], all expressed as iprodione equivalents
Codex	Iprodione

[1] The residue definition (RD) assumed for the risk assessment is iprodione for all plant commodities except rice, where the residue definition is iprodione and RP30228. For animal matrices except (milk), the RD for the risk assessment is iprodione, RP30228, and RP32490. For milk, the RD for the risk assessment is iprodione, RP30228, RP32490, and RP36114.

Appendix VIII Environmental Fate, Behaviour, Toxicity and Risk Asessment of Iprodione

Table 1 Fate and Behaviour of Iprodione in the Environment

Study type	Test material	Study Conditions	Value	Interpretation	Major transformation products	Reference
Abiotic transformation						
Hydrolysis	Iprodione	25 °C; 30 d	Half-life: pH 5: 130.7d pH 7: 6.4 d pH 9: 27.2 min.	Not a major route of transformation under acidic conditions	RP35606 at pH 5 and 7; RP30228 at pH 7 and 9	PMRA 1183191
Phototransformation on soil	Iprodione	25 °C; 30 d Sandy loam, pH: 6.9, OM: 1.34%	Half-life: 7 – 14 d	Not a major route of transformation	RP32596 (3,5-DCA)	PMRA 1183199
Phototransformation on water	Iprodione	25 °C, pH 5, 30 d	Half-life: 67 d	Not a major route of transformation	No major transformation products (>10% AR) were identified.	PMRA 1183202
Biotransformation						
Soil - aerobic	Iprodione	276 days; sandy loam soil; 25°C; pH 6.08; % OM 1.28	DT50: 16.3 d	Slightlypersistent	No major transformation products (>10% AR) were identified.	PMRA 1759501
		385 days; clay loam soil; 25°C; pH 7.0; %OM 4.0; (10 ppm iprodione treatment)	DT50: 83.8	Moderately persistent	RP30228	PMRA 1183210
		385 days; clay loam soil; 25°C; pH 7.0; %OM 4.0; (1 ppm iprodione treatment)	DT50: 43.3	Slightlypersistent	No major transformation products (>10% AR) were identified.	
		385 days; silty clay soil; 25°C; pH 7.6; % OM 3.1	DT50: 25.6	Slightlypersistent	RP30228	

Study type	Test material	Study Conditions	Value	Interpretation	Major transformation products	Reference
		367 days, clay loam soil, 15°C; pH 7.0; %OM 4.0	DT50: 174	Moderately persistent	RP30228	
		Loam	DT50: 38.4	Slightly persistent	RP30228	PMRA 1165211
		Loam	DT50: 41	Slightly persistent	RP30228	
Soil - anaerobic	Iprodione	Silt loam	DT50: 7 – 14 d	Non persistent	RP30228	PMRA 1794765
		Clay loam	DT50: 21 – 26	Slightly persistent	RP30228	PMRA 1165210
Water/sediment - aerobic	Iprodione	30 days, 25°C; silt loam; %OM 1.55; water pH 8.5	whole system DT50: 6.1 d water phase DT50: 0.6 d	Non-persistent	RP30228 and RP32490	PMRA 1165213
		100 days, 20°C Two systems: Mill stream pond and Iron Hatch pool runoff; water pH range 7.1-8.2 (pH 7.9 at test initiation)	DT50: <6 hours (water phase)	Non persistent	RP30228 and RP36006	PMRA 1165214
Water/sediment-anaerobic	Iprodione	365 d, 25 °C; silt loam; %OM 2.0; pH 7.4	whole system DT50: 11.7 d water phase DT50: 2.5 d	Non-persistent	RP30228	PMRA 1162248
Mobility						
Adsorption/ desorption	Iprodione	Four soils: pH 5.9 – 7.8; % OM 0.2 – 14.8	K_d = 0.21 – 44.31 K_{OC} = 204 – 543	Low to moderate mobility; adsorption was correlated with organic carbon content	Not reported	PMRA 1162263
	RP30228		K_d = 64 to 127 K_{oc} = 5472 to 10056	Immobile?	Not reported	PMRA 1759505

Study type	Test material	Study Conditions	Value	Interpretation	Major transformation products	Reference
	RP32595 (3,5-DCA)		K_d = 2.6 to 17.9 K_{oc} = 690 to 1346	Low to medium mobility†	Not reported	PMRA 1759504
Soil column leaching	Iprodione	Four soils: pH 5.97 – 7.8; % OM 0.2 – 2.1	Majority of iprodione applied to soil did not leach beyond 20 cm soil depth, (< 3% of AR detected in leachate), with the exception of sand soil that is low in organic matter (12.7 – 52% AR in leachate from sand soil; ~0.2% OM).		RP35606 and RP30228	PMRA 1759505
Field studies						
Field dissipation	Iprodione	California: silt loam	$T_{1/2}$: 7 d No residues were detected below 30 cm depth in soil	Non persistent	RP30228	PMRA 1759517
		North Carolina: loamy sand	$T_{1/2}$: < 3 d No residues were detected below 15 cm depth in soil	Non persistent	RP30228	
		Western Europe: Goch, Germany; Lyon, southern France; Mannigtree, UK and Seville, Spain	DT50: 8.7 – 19 d No residues were detected below 30 cm depth in soil	Non persistent	RP30228	PMRA 1759512

† Classified according to McCall et al. 1981.

Table 2 Major Transformation Products of Iprodione

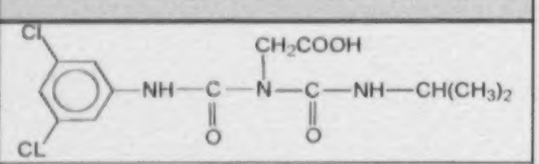
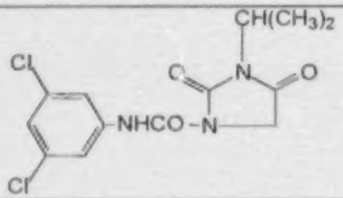
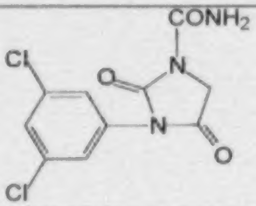
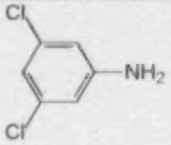
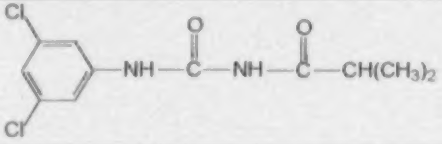
Transformation Product	Chemical name	Chemical structure
RP35606	[(dichloro-3,5-phenyl)- 1 - isopropylcarbamoyl-3]-2-acetic acid	
RP30228	3-(1 -methylethyl)-N-(3, 5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboxamide	
RP32490	3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboxamide	
RP32596	3,5-dichloroaniline (DCA)	
RP36221		

Table 3 Toxicity of Iprodione to Non-Target Species

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Effect of concern	Reference
Terrestrial Organisms							
Soil dwelling organisms	Field study	(*Apporretodea* and *Lumbricus terrestris* adults or juveniles)	50% WP formulation	89-d NOEC	12kg a.i./ha	Mortality/biomass	PMRA 1220782
	Acute	springtails (*Folsomia candida*)	Technical (97% purity)	24-h LD_{50}	>100 mg a.i./kg soil	Mortality	
		Earthworm (*Eisenia fetida*)	Formulation (purity 961 g/kg)	14-d LD_{50}	>1000 mg a.i./kg soil	Mortality	PMRA 1759526
	Chronic	Earthworm (*Eisenia andrei*)		8- week NOEC	1000 mg a.i./kg soil	Mortality/biomass	PMRA 1759524
	Chronic	Earthworm (*Eisenia andrei*)	RP 30228	8- week NOEC	1000 mg a.i./kg soil		PMRA 1759523
		Earthworm (*Eisenia fetida*)	3,5-DCA (RP32596)	8- week NOEC	100 mg a.i./kg soil		PMRA 1759525
Bee	Contact	Honey bee (*Apis mellifera*)	Technical (% a.i. not reported)	LD_{50}	> 120 µg a.i./bee	mortality	PMRA 1794743
				24-h LD_{50}	> 200 µg a.i./bee		PMRA 1183269
	Oral		Technical (97.1 % purity)	24-h LD_{50}	> 25 µg a.i./bee		
Beneficial arthropods	Contact	*Typhlodromus pyri*	Formulation (purity 508 g/kg)	LR_{50}	< 750 g a.i./ha	Mortality	PMRA 1759528
		Aphidus rhopalosiphi	NR	LR_{50}	< 750 g a.i./ha	Mortality	PMRA 1794745
Birds	Acute	northern bobwhite quail (*Colinus virginuanus*)	Technical (96.2% purity)	LD_{50}	>2000 mg a.i./kg bw	Mortality	PMRA 1759553
		northern bobwhite quail (*Colinus virginuanus*)	Technical	LD_{50}	930 mg a.i./kg/bw	Mortality	PMRA 1794743
		mallard duck (*Anas platyrhynchos*)	Technical	LD_{50}	10437 mg a.i./kg/bw		PMRA 1759554

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Effect of concern	Reference
	Dietary	northern bobwhite quail (*Colinus virginuanus*)	Technical (96.2% purity)	5-d LD$_{50}$	> 5620 mg a.i./kg diet (>4121 mg a.i./kg bw/day)	Mortality	PMRA 1759555
		mallard duck (*Anas platyrhynchos*)	Technical (96.2% purity)	5-d LD$_{50}$	> 5620 mg a.i./kg diet (>1297 mg a.i./kg bw/day)		PMRA 1759556
	Reproduction	northern bobwhite quail (*Colinus virginuanus*)	Technical (96.2% purity)	22-week NOEL	300 mg a.i./kg diet (22 mg a.i./kg bw/day)	Endpoints affected: Hatchling body weight	PMRA 1759559
		mallard duck (*Anas platyrhynchos*)	Technical (96.2% purity)	22-week NOEL	300 mg a.i./kg diet (26 mg a.i./kg bw/day)	Endpoints affected: fewer 14-day old survivors	PMRA 1759557
Mammals	Acute	CD-1 mouse	NR	LD$_{50}$	1870 / 2670 (♂/♀) mg/kg bw	Mortality	PMRA 1711132
		CD Rat	NR	LD$_{50}$	2060 / 1530 (♂/♀) mg/kg bw		PMRA 1711131
		Wistar rat	NR	LD$_{50}$	3700 mg/kg bw		PMRA 1711129
		CD-2 mouse CD rat	Technical	LD$_{50}$	4000 mg/kg bw >2000 mg/kg bw		PMRA 1711116
	dietary	CF-1 Mouse	NR	4-week NOEL	1500 mg ai/kg bw/day	Endpoints affected: Based on mortality and reduced body weight	PMRA 1816255
		CF-1 Carworth Mouse			1860 / 2090 (♂/♀) mg ai/kg bw/day		
		CD-1 mouse	Technical (95.7% purity)		900 mg a.i./kg/day		PMRA 1711136
		CD-1 mouse		13 week NOEL	1110 / 1300 (♂/♀) mg ai/kg bw/day		PMRA 1611932
		SD rat		13 week NOEL	78 / 89 (♂/♀) mg ai/kg bw/day	Endpoints affected: Based on reduced body weight and body weight gain	PMRA 1611930
		CD/CRJ rat	NR	13 week NOEL	21 / 24 (♂/♀) mg ai/kg bw/day	Endpoints affected: Based on reduced body weight	PMRA 1711135
		SD rat	NR	13-week NOEL	31 / 36 (♂/♀) mg ai/kg bw/day	Endpoints affected: Based on reduced body weight	PMRA 1711117

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Effect of concern	Reference
	2 generation reproduction	Crl:CD BR/VAF/PLUS rats	Technical (96.2% purity)	NOEL	parental: 21 Repro: 68 / 82 offspring: 68 / 82 (mg a.i./kg bw/day)	Endpoints affected: Based on reduced body weight and body weight gain	1166135 & 1166136
Vascular plants	NA						
Freshwater Organisms							
Invertebrates	Acute	*Daphnia magna*	Technical (96.2% purity)	48-h LC_{50}	240 µg a.i./L (mean measured)	mortality	PMRA 1759534
			Technical (94.5% purity)	48-h LC_{50}	430 µg a.i./L (nominal)		PMRA 1794743
					7200 µg a.i./L (nominal)		
			50% formulation		360 µg a.i./L (mean measured)		
		Daphnia pulex		72-h LC_{50}	5800 µg a.i./L (nominal)		
			Technical (purity not reported)		4000 µg a.i./L (nominal)		
		Juvenile crayfish (*Procambarus simulans*)	Technical (95% purity)	7-d	> 4100 µg a.i./L (mean measured)		PMRA 1759536
	Chronic	*Daphnia magna*	Technical (100% purity)	21-d NOEC	170 µg a.i./L (mean measured)	Offspring/female, mean percentage survival, growth	PMRA 1759535
		sediment dwelling organism *Chironomus riparius*	RP30228 (purity 999 g/kg)	28-d NOEC (limit test)	>100 µg a.i./L (nominal)	Emergence of adult midges from 1^{st} instar larvae	PMRA 1759537
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Technical (96.2% purity)	96-h LC_{50}	4100 µg a.i./L (mean measured)	Mortality	PMRA 1759544
			Technical (95.1% purity)		4200 µg a.i./L (nominal)		PMRA 1759542

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Effect of concern	Reference
			RP30228 (98% purity)		>400 µg a.i./L (mean measured)		PMRA 1770949
		Bluegill sunfish *(Lepomis macrochirus)*	Technical (95.1% purity)		6300 µg a.i./L (nominal)		PMRA 1759547
			Technical (96.2% purity)		3700 µg a.i./L (mean measured)		PMRA 1759546
			50% formulation		7800 µg a.i./L (mean measured)		PMRA 1764783
			RP30228 (purity not reported)		550 µg a.i./L (not reported)		PMRA 1764785
		Channel catfish *(Ictalurus punctatus)*	Technical (95% purity)		3100 µg a.i./L (mean measured)		PMRA 1759547
	Chronic	Fathead minnow *(Pimephales promelas)*	Technical (100% purity)	34 day early life stage NOEC LOEC	260 µg a.i./L 550 µg a.i./L (mean measured)	Larval survival	PMRA 1759549
Algae	Acute	Freshwater diatom *(Navicula pelliculosa)*	Technical (96.2% purity)	120-h EC_{50} NOEC	48 µg a.i./L 13 µg a.i./L (mean measured)	Biomass / growth rate	PMRA 1759560
		Green algae *(Scenedesmus subspicatus)*	Formulation (225 g/L iprodione)	72-h EC_{50} NOEC	3100 µg a.i./L 5700 µg a.i./L 2100 µg a.i./L (mean measured)	Biomass / growth rate	PMRA 1759563
			NR	EC_{50}	500 µg a.i./L	NR	PMRA 1759563
		Green algae *(Selenastrum capricornutum)*	Technical (96.2% purity)	120-h EC_{50} NOEC	2000 µg a.i./L 140 µg a.i./L (mean measured)	Biomass / growth rate	PMRA 1764785
		Green algae *(Anabaena flos-aquae)*	Technical (96.2% purity)	120-h EC_{50} NOEC	>1300 µg a.i./L 1300 µg a.i./L (mean measured)	Biomass / growth rate	PMRA 1759564

Organism	Study type	Species	Test material	Endpoint	Value (nominal / mean measured)	Effect of concern	Reference
Vascular Plants	Acute	Duckweed (*Lemna gibba*)	Technical (97.8% purity)	7-d EC50 NOEC	[illegible] µg a.i./L [illegible] µg a.i./L (mean measured)	Growth inhibition: biomass, frond number	PMRA [illegible]
			Technical (96.2% purity)	14-d EC50 NOEC	[illegible] µg a.i./L [illegible] µg a.i./L (mean measured)	Growth inhibition: frond number	PMRA [illegible]
Marine and estuarine Organisms							
Invertebrates	Acute	Mysid shrimp (*Mysidopsis bahia*)	Technical (100% purity)	96-h EC50	[illegible] µg a.i./L (mean measured)	Mortality	PMRA [illegible]
		Eastern oyster (*Crassostrea virginica*)	Technical (95% purity)	96-h EC50	[illegible] µg a.i./L (mean measured)	Shell deposition	PMRA [illegible]
	Chronic	Mysid shrimp (*Mysidopsis bahia*)	Technical (100% purity)	28-d NOEC LOEC	[illegible] µg a.i./L [illegible] µg a.i./L	Offspring/female/reproductive day	PMRA [illegible]
Fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	Technical (95% purity)	96-h LC50	[illegible] µg a.i./L (mean measured)	Mortality	PMRA [illegible]
Algae	Acute	Marine diatom (*Skeletonema costatum*)	Technical (96.2% purity)	EC50 NOEC	[illegible] µg a.i./L [illegible] µg a.i./L	Growth inhibition	PMRA [illegible]

NR – not reported

Table 4 Avian Risk Assessment Using Mean Iprodione Residue Values Based on The Maximum Cumulative Agricultural Rate (Raspberry – 1000 g a.i./ha × 8 at 7-day intervals) the Highest Application Rate for Turf Use (9000 g a.i./ha × 3 @ 14-day Intervals)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg ai/kg bw/d)	Food Guild (food item)	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ
raspberry – 1000 g ai/ha × 8 at 7 day intervals										
Small Bird (0.02 kg)										
Acute	93	Insectivore	207	2.2	153	1.7	143	1.5	106	1.1
Reproduction	22	Insectivore	207	9.4	153	7.0	143	6.5	106	4.8
		Granivore (grain and seeds)	32	1.5	24	1.1	15	0.7	11	0.5
		Frugivore (fruit)	64	2.9	48	2.2	31	1.4	23	1.0
Medium Sized Bird (0.1 kg)										
Acute	93	Insectivore	162	1.7	120	1.3	112	1.2	83	0.9
Reproduction	22	Insectivore	162	7.4	120	5.4	112	5.1	83	3.8
		Granivore (grain and seeds)	25	1.1	19	0.8	12	0.5	8.8	0.4
		Frugivore (fruit)	50	2.3	37	1.7	24	1.1	18	0.8
Large Sized bird (1 kg)										
	93	Herbivore (short grass)	105	1.1	77	0.8	37	0.4	27	0.3
		Herbivore (Broadleaf plants)	97	1.0	72	0.8	32	0.3	24	0.3
Reproduction	22	Insectivore	47	2.2	35	1.6	33	1.5	24	1.1
		Herbivore (short grass)	105	4.8	77	3.5	37	1.7	27	1.3
		Herbivore (long grass)	64	2.9	47	2.2	21	0.9	15	0.7
		Herbivore (Broadleaf plants)	97	4.4	72	3.3	32	1.5	24	1.1
turf use - 9000 g a.i./ha × 3 at 14 d intervals										
Large Sized Bird (1 kg)										
Acute	93	Herbivore (short grass)	562	6.1	34	0.4	200	2.15	12	0.1
Reproduction	22	Herbivore (short grass)	562	26	34	1.5	200	9.08	12	0.5

Table 5 Mammalian Risk Assessment Using Mean Iprodione Residue Values Based on the maximum Cumulative Agricultural Rate (Raspberry – 1000 g a.i./ha × 8 at 7-day intevals) the Highest Application Rate for Turf Use (9000 g a.i./ha × 3 at 14-day Intervals)

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg ai/kg bw/d)	Food Guild (food item)	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ	EDE (mg ai/kg bw)	RQ
raspberry – 1000 g ai/ha × 8 at 7 day intevals										
Small Mammal (0.015 kg)										
Reproduction	68	Insectivore	119	1.8	88	1.3	82	1.2	61	0.9
Medium Sized Mammal (0.035 kg)										
Reproduction	68	Insectivore	105	1.5	77	1.1	72	1.1	53	0.8
		Herbivore (short grass)	231	3.4	171	2.5	82	1.2	61	0.9
		Herbivore (long grass)	141	2.1	105	1.5	46	0.7	34	0.5
		Herbivore (Broadleaf plants)	214	3.1	158	2.3	71	1.0	52	0.8
Large Sized Mammal (1 kg)										
Reproduction	68	Herbivore (short grass)	124	1.8	91	1.3	44	0.6	32	0.5
		Herbivore (long grass)	75	1.1	56	0.8	25	0.4	18	0.3
		Herbivore (Broadleaf plants)	114	1.7	85	1.2	38	0.6	28	0.4
turf use - 9000 g a.i. / ha × 3 at 14 d intervals										
Medium Sized Mammal (0.035 kg)										
Acute	153.00	Herbivore (short grass)	1244	8.1	75	0.5	442	2.9	27	0.2
Reproduction	68.00	Herbivore (short grass)	1244	18	75	1.1	442	6.5	27	0.4
Large Sized Mammal (1 kg)										
Acute	153.00	Herbivore (short grass)	665	4.3	40	0.3	236	1.5	14	0.1
Reproduction	68	Herbivore (short grass)	665	9.8	40	0.6	236	3.5	14	0.2

Table 6 The Number of Seeds Treated with Iprodione Required to Reach the Bird and Mammalian Endpoints

Endpoint	Weight (g)	Number of seeds to reach endpoint		
		Carrot	Canola	Mustard
Birds				
Acute 93 mg a.i./kg bw	20	620	169	332
	100	3100	845	1661
	1000	31000	8455	16607
Dietary 130 mg a.i./kg bw/day	20	867	236	464
	100	4333	1182	2321
	1000	43333	11818	23214
Reproduction 22 mg a.i./kg bw/day	20	147	40	71
	100	733	200	393
	1000	7333	2000	3929
Mammals				
Acute 153 mg a.i./kg bw	15	765	209	546
	35	1785	489	956
	1000	51000	13909	27321
Dietary 78 mg a.i./kg bw/day	15	390	106	209
	35	910	248	488
	1000	26000	7091	13929
Reproduction 68 mg a.i./kg bw/day	15	340	93	182
	35	793	216	425
	1000	22667	6181	12143

[1] # seeds/day to reach endpoint = Dose-based endpoint × BW (kg bw) ÷ concentration per seed (mg a.i./seed)

Table 7 Generic bird and mammal seed consumption per day

Species	FIR (g dw/day)	(# seeds consumed/day)		
		Carrot	Canola	Mustard
Small bird – 20 g	5.1	4137	1275	2698
Medium bird – 100 g	19.9	16143	4975	10527
Large bird – 1000 g	58.1	47131	14525	30735
Small mammal – 15 g	2.2	1785	550	1164
Medium mammal – 35 g	4.5	3650	1125	2381
Large mammal – 1000 g	68.7	55730	17175	36342

[1] The number of seeds normally consumed per day was calculated as: # seeds consumed/day = FIR (g dw/day) × # seeds/g; for each body weight, the food ingestion rate is based on equations from Nagy (1987).

Table 8 Screening level risk quotients for birds and mammals consuming treated seeds.

Endpoint	Weight (g)	Risk quotients		
		Carrot	Canola	Mustard
Birds				
Acute 93 mg a.i./kg bw	20	7	8	8
	100	5	6	6
	1000	2	2	2
Dietary 130 mg a.i./kg bw/day	20	5	5	6
	100	4	4	5
	1000	1	1	1
Reproduction 22 mg a.i./kg bw/day	20	37	41	44
	100	28	32	35
	1000	8	9	10
Mammals				
Acute 153 mg a.i./kg bw	15	2	3	2
	35	2	2	2
	1000	1	1	1

Endpoint	Weight (g)	Risk quotients		
		Carrot	Canola	Mustard
Dietary 78 mg a.i./kg bw/day	15	5	5	6
	35	4	5	5
	1000	2	2	3
Reproduction 68 mg a.i./kg bw/day	15	5	6	6
	35	5	5	6
	1000	2	3	3

[1] Risk quotients calculated as: # of seeds normally consumed per day (Table 15) ÷ # of seeds to the endpoint (Table 14); risk quotients >1 exceed the level of concern.

Table 9 Area covered necessary to reach toxic quantities assuming only 3.3% of planted seeds are available to birds and mammals

Endpoint	Weight (g)	#seeds to reach LOC / m^2 required to reach LOC [1]		
		Carrot	Canola	Mustard
Birds				
Acute 93 mg a.i./kg bw	20	620 / 52	169 / 19	332 / 17
	100	3100 / 258	845 / 97	1661 / 85
	1000	31000 / 2583	8455 / 972	16607 / 847
Dietary 130 mg a.i./kg bw/day	20	867/ 72	236 / 27	464 / 24
	100	4333 / 498	1182 / 136	2321 / 118
	1000	43333 / 2210	11818 / 1358	23214 / 1184
Reproduction 22 mg a.i./kg bw/day	20	147 / 12	40 / 5	71 / 4
	100	733 / 61	200 / 23	393 / 20
	1000	7333 / 611	2000 / 230	3929 / 200
Mammals				
Acute 153 mg a.i./kg bw	15	765 / 64	209 / 24	546 / 28
	35	1785 / 149	489 / 56	956 / 49
	1000	51000 / 4250	13909 / 1599	27321 / 1394
Dietary 78 mg a.i./kg bw/day	15	390 / 33	106 / 12	209 / 11
	35	910 / 76	248 / 29	488 / 25
	1000	26000 / 2166	7091 / 815	13929 / 711
Reproduction 68 mg a.i./kg bw/day	15	340 / 28	93 / 11	182 / 9
	35	793 / 66	216 / 25	425 / 22
	1000	22667 / 1889	6181 / 710	12143 / 620

[1] m^2 required to reach LOC = number seeds to reach LOC / maximum seed density available in spring (3.3%); m^2 values are rounded off to nearest m^2.

Table 10 The number of treated granules required to reach the bird and mammalian endpoints

Endpoint	Weight (g)	Number of granules to reach endpoint
Birds		
Acute 93 mg a.i./kg bw	20	930
	100	4650
	1000	46500
Dietary 130 mg a.i./kg bw/day	20	1300
	100	6500
	1000	65000
Reproduction 22 mg a.i./kg bw/day	20	220
	100	1100
	1000	11000
Mammals		
Acute 153 mg a.i./kg bw	15	1148
	35	2678
	1000	76500
Dietary	15	585

Endpoint	Weight (g)	Number of granules to reach endpoint
78 mg a.i./kg bw/day	35	1365
	1000	39000
Reproduction 68 mg a.i./kg bw/day	15	510
	35	1190
	1000	34000

[1] # granules/day to reach endpoint = Dose-based endpoint × BW (kg bw) ÷ concentration per granule (mg a.i./granule).

Table 11 Generic bird and mammal granule consumption per day

Species	FIR (g dw/day)	(# granules consumed/day)
Small bird – 20 g	5.1	31824
Medium bird – 100 g	19.9	124176
Large bird – 1000 g	58.1	362544
Small mammal – 15 g	2.2	13728
Medium mammal – 35 g	4.5	28080
Large mammal – 1000 g	68.7	428688

[1] The number of granules normally consumed per day was calculated as:
# granules consumed/day = FIR (g dw/day) × # of granules/g of product; for each body weight, the food ingestion rate is based on equations from Nagy (1987).

Table 12 Screening level risk quotients for birds and mammals consuming treated granules.

Endpoint	Weight (g)	Risk quotients
Birds		
Acute 93 mg a.i./kg bw	20	34
	100	27
	1000	8
Dietary 130 mg a.i./kg bw/day	20	24
	100	19
	1000	6
Reproduction 22 mg a.i./kg bw/day	20	145
	100	113
	1000	33
Mammals		
Acute 153 mg a.i./kg bw	15	12
	35	10
	1000	6
Dietary 78 mg a.i./kg bw/day	15	23
	35	21
	1000	11
Reproduction 68 mg a.i./kg bw/day	15	27
	35	24
	1000	13

[1] Risk quotients calculated as: # of granules normally consumed per day (Table 19) ÷ # of granules to the endpoint (Table 18); risk quotients >1 exceed the level of concern.

Table 13 Risk Quotients for Mammals Based on an Estimate of Incidental Granule Consumption as 1% of the EDE

Endpoint	Weight (g)	Risk quotients
Acute 153 mg a.i./kg bw	15	0.1
	35	0.1
	1000	<0.1
Dietary 78 mg a.i./kg bw/day	15	0.2
	35	0.2
	1000	<0.1
Reproduction 68 mg a.i./kg bw/day	15	0.3
	35	0.2
	1000	<0.1

Table 14 Summary of Screening Level Risk Assessment of Iprodione and the Transformation Product RP30228 to Aquatic Organisms

Organism	Exposure	Species	Endpoint value (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use Rate[2] (g a.i./ha)	EEC[3] (µg a.i./L)	RQ	LOC Exceeded
Iprodione - Freshwater species								
Invertebrate	Acute	*Daphnia magna*	48-h LC$_{50}$ = 240	120	744 (alfalfa)	90	0.7	No
					1000 × 8 (raspberry)	230	**1.9**	Yes
					9000 × 3 (turf)	1400	**12**	Yes
	Chronic	*Daphnia magna*	21-d NOEC = 170	170	744 (alfalfa)	90	0.5	No
					1000 × 8 (raspberry)	230	**1.4**	Yes
					9000 × 3 (turf)	1400	**8.2**	Yes
Fish	Acute	Channel catfish *(Ictalurus punctatus)*	96 -h LC$_{50}$ = 3100	310	744 (alfalfa)	90	0.3	No
					1000 × 8 (raspberry)	230	0.7	No
					9000 × 3 (turf)	1400	**4.5**	Yes
	Chronic	Fathead minnow *(Pimephales promelas)*	34-d ELS NOEC = 260	260	744 (alfalfa)	90	0.3	No
					1000 × 8 (raspberry)	230	0.9	No
					9000 × 3 (turf)	1400	**5.4**	Yes
Amphibians	Acute	Surrogate fish *(Ictalurus punctatus)*	96 -h LC$_{50}$ = 3100	310	744 (alfalfa)	500	**1.6**	Yes
					1000 × 8 (raspberry)	1210	**3.9**	Yes
					9000 × 3 (turf)	7470	**24**	Yes
	Chronic	Surrogate fish *(Pimephales promelas)*	34-d ELS NOEC = 260	260	744 (alfalfa)	500	**1.9**	Yes
					1000 × 8 (raspberry)	1210	**4.7**	Yes
					9000 × 3 (turf)	7470	**29**	Yes
Freshwater alga	Acute	Freshwater diatom *(Navicula pelliculosa)*	120-h EC$_{50}$ = 48	24	744 (alfalfa)	90	**3.8**	Yes
					1000 × 8 (raspberry)	230	**10**	Yes
					9000 × 3 (turf)	1400	**58**	Yes

Organism	Exposure	Species	Endpoint value (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use Rate[2] (g a.i./ha)	EEC[3] (µg a.i./L)	RQ	LOC Exceeded
Vascular plant	Acute	Duckweed *(Lemna gibba)*	14-d EC_{50} = 12640	6320	744 (alfalfa)	90	0.01	No
					1000 × 8 (raspberry)	230	0.04	No
					9000 × 3 (turf)	1400	0.22	No
Iprodione - Estuarine and marine species								
Invertebrate	Acute	Mysid shrimp *(Mysidopsis bahia)*	96-h LC_{50} = 680	340	744 (alfalfa)	90	0.2	No
					1000 × 8 (raspberry)	230	0.7	No
					9000 × 3 (turf)	1400	**4.1**	Yes
	Chronic	Mysid shrimp *(Mysidopsis bahia)*	21-d NOEC = 3.5	3.5	744 (alfalfa)	90	**26**	Yes
					1000 × 8 (raspberry)	230	**66**	Yes
					9000 × 3 (turf)	1400	**400**	Yes
Mollusk	Acute	Eatern Oysters *(Crassostrea virginica)*	96-h LC_{50} = 2300	1150	744 (alfalfa)	90	<0.1	No
					1000 × 8 (raspberry)	230	0.2	No
					9000 × 3 (turf)	1400	**1.2**	Yes
Fish	Acute	Sheepshead minnow *(Cyprinodon variegates)*	96-h LC_{50} = 7700	770	744 (alfalfa)	90	0.1	No
					1000 × 8 (raspberry)	230	0.3	No
					9000 × 3 (turf)	1400	**1.8**	Yes
Marine alga	Acute	Marine diatom *(Skeletonema costatum)*	120-h LC50 = 330	165	744 (alfalfa)	90	0.5	No
					1000 × 8 (raspberry)	230	**1.4**	Yes
					9000 × 3 (turf)	1400	**8.5**	Yes
RP30228 – freshwater organisms								
Sediment dwelling organism	Chronic	*Chironomus riparius*	21-d NOEC ≥ 100	100	744 (alfalfa)	90	0.9	No
					1000 × 8 (raspberry)	1000	**10**	Yes
					9000 × 3 (turf)	3380	**34**	Yes
Fish	Acute	Bluegill sunfish *(Lepomis macrochirus)*	96-h LC_{50} =550	55	744 (alfalfa)	90	**1.6**	Yes
					1000 × 8 (raspberry)	1000	**18**	Yes
					9000 × 3 (turf)	3380	**61**	Yes
Amphibians	Acute	Bluegill sunfish *(Lepomis macrochirus)*	96-h LC_{50} =550	55	744 (alfalfa)	500	**9.1**	Yes
					1000 × 8 (raspberry)	5330	**97**	Yes
					9000 × 3 (turf)	18000	**327**	Yes

[1] Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

[2] Application rate represents the lowest single application for alfalfa (744 g a.i./ha), highest cumulative application rate for raspberry (1000 g a.i./ha × 8 at 7 day intervals) and the highest cumulative rate for turf use (9000 g a.i./ha × 6 at 14 day intervals).

[3] EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic.

Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 15 Spray Drift Assessment of Iprodione and RP 30228 to Non-target Aquatic Organisms Using Percent Drift Deposition

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA* (µg a.i./L)	Use Scenario (rate - g a.i./ha)**	EEC Exposure from drift (µg a.i./L)	RQ	LOC exceeded
Iprodione - Freshwater species								
Freshwater Invertebrate	Acute	*Daphnia magna*	48-h LC$_{50}$ = 240	120	Ground - strawberry (1000 × 8, 7d)	14	0.1	No
					Aerial – snap beans (750 × 2, 7d)	31	0.3	No
					Airblast - raspberry (1000 × 8, 7d)	168	**1.4**	Yes
					Turf (9000 × 3, 14d)	84	0.7	No
	Chronic	*Daphnia magna*	21-d NOEC = 170	170	Ground - strawberry (1000 × 8, 7d)	14	<0.1	No
					Aerial – snap beans (750 × 2, 7d)	31	0.2	No
					Airblast - raspberry (1000 × 8, 7d)	168	0.9	No
					Turf (9000 × 3, 14d)	84	0.5	No
Freshwater fish	Acute	Channel catfish (*Ictalurus punctatus*)	96 - h LC$_{50}$ = 3100	310	Ground - strawberry (1000 × 8, 7d)	14	<0.1	No
					Aerial – snap beans (750 × 2, 7d)	31	0.1	No
					Airblast - raspberry (1000 × 8, 7d)	168	0.5	No
					Turf (9000 × 3, 14d)	84	0.3	No
	Chronic	Fathead minnow (*Pimephales promelas*)	34-d ELS NOEC = 260	260	Ground - strawberry (1000 × 8, 7d)	14	<0.1	No
					Aerial – snap beans (750 × 2, 7d)	31	0.1	No
					Airblast - raspberry (1000 × 8, 7d)	168	0.6	No
					Turf (9000 × 3, 14d)	84	0.3	No

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RQ* (µg a.i./L)	Use Scenario (rate × #, RI days)**	EEC Exposure from drift (µg a.i./L)	RQ	LOC exceeded
Amphibian	Acute	Surrogate fish *(Ictalurus punctatus)*	96-h LC$_{50}$ = 3100	310	Ground - strawberry (1000 × 8, 7d)	73	0.2	No
					Aerial - snap beans (750 × 2, 7d)	167	0.5	No
					Airblast - raspberry (1000 × 8, 7d)	898	**2.9**	Yes
					Turf (9000 × 3, 14d)	448	**1.4**	Yes
	Chronic	Surrogate fish *(Pimephales promelas)*	34-d ELS NOEC = 260	260	Ground - strawberry (1000 × 8, 7d)	73	0.3	No
					Aerial - snap beans (750 × 2, 7d)	167	0.6	No
					Airblast - raspberry (1000 × 8, 7d)	898	**3.5**	Yes
					Turf (9000 × 3, 14d)	448	**1.7**	Yes
Freshwater alga	Acute	Freshwater diatom *(Navicula pelliculosa)*	120-h EC$_{50}$ = 48	24	Ground - strawberry (1000 × 8, 7d)	14	0.6	No
					Aerial - snap beans (750 × 2, 7d)	31	**1.3**	Yes
					Airblast - raspberry (1000 × 8, 7d)	168	**7.0**	Yes
					Turf (9000 × 3, 14d)	84	**3.5**	Yes
Iprodione - Estuarine and marine species								
Invertebrate	Acute	Mysid shrimp *(Mysidopsis bahia)*	96-h LC$_{50}$ = 680	340	Ground - strawberry (1000 × 8, 7d)	14	<0.1	No
					Aerial - snap beans (750 × 2, 7d)	31	<0.1	No
					Airblast - raspberry (1000 × 8, 7d)	168	0.5	No
					Turf (9000 × 3, 14d)	84	0.2	No
	Chronic	Mysid shrimp *(Mysidopsis*	21-d NOEC = 3.7	3.7	Ground - strawberry (1000 × 8, 7d)	14	**3.8**	Yes

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RQ¹ (µg a.i./L)	Use Scenario (Rate - g a.i./ha)¹²	EEC (Aqueous from drift (µg a.i./L))	RQ	LOC exceeded
		Salina			Aerial - snap beans (750 × 2, 7d)	33	6.6	Yes
					Airblast - raspberry (1000 × 8, 7d)	108	22	Yes
					Turf (10000 × 3, 14d)	64	13	Yes
Mollusk	Acute	Eastern Oyster (*Crassostrea virginica*)	96-h EC₅₀ = 2300	1150	Ground - strawberry (1000 × 8, 7d)	18	<0.1	No
					Aerial - snap beans (750 × 2, 7d)	33	<0.1	No
					Airblast - raspberry (1000 × 8, 7d)	108	0.1	No
					Turf (10000 × 3, 14d)	64	<0.1	No
Marine estuarine fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	96-h LC₅₀ = 7700	770	Ground - strawberry (1000 × 8, 7d)	18	<0.1	No
					Aerial - snap beans (750 × 2, 7d)	33	<0.1	No
					Airblast - raspberry (1000 × 8, 7d)	108	0.2	No
					Turf (10000 × 3, 14d)	64	0.1	No
Marine algae	Acute	Marine diatom (*Skeletonema costatum*)	120-h EC₅₀ = 330	107	Ground - strawberry (1000 × 8, 7d)	18	<0.1	No
					Aerial - snap beans (750 × 2, 7d)	33	0.2	No
					Airblast - raspberry (1000 × 8, 7d)	108	**1.0**	Yes
					Turf (10000 × 3, 14d)	64	0.5	No
SDS-3701 – Freshwater organisms								
Sediment dwelling invertebrate	Chronic	*Chironomus riparius*	28-d NOEC = 100	100	Ground - strawberry (1000 × 8, 7d)	11	0.1	No
					Aerial - snap beans (750 × 2, 7d)	27	0.3	No

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA* (µg a.i./L)	Drift Scenario** [illegible]	EEC (Exposure from drift) (µg a.i./L)	RQ	LOC exceeded
					Airblast - [illegible]	[illegible]	**[illegible]**	Yes
					Aerial [illegible]	[illegible]	[illegible]	No
Fish	Acute	Bluegill sunfish (*Lepomis macrochirus*)	96-h LC50 = [illegible]	[illegible]	Ground - [illegible]	[illegible]	[illegible]	No
					Airblast - [illegible]	[illegible]	[illegible]	No
					Airblast - [illegible]	[illegible]	**[illegible]**	Yes
					Aerial [illegible]	[illegible]	**[illegible]**	Yes
Amphibians	Acute	Surrogate fish (*Lepomis macrochirus*)	96-h LC50 = [illegible]	[illegible]	Ground - [illegible]	[illegible]	**[illegible]**	Yes
					Airblast - [illegible]	[illegible]	**[illegible]**	Yes
					Airblast - [illegible]	[illegible]	**[illegible]**	Yes
					Aerial [illegible]	[illegible]	**[illegible]**	Yes

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC50, LC50 from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

** The assessment of potential risk from drift was assessed for the highest cumulative application rate as listed on the labels specific to each of the three application methods. An assumption of medium spray droplets is made for fungicides applied using conventional methods. Drift: sprayer (6%), aerial (23%), and airblast (74% for early season application).

Risk quotients shown in bold exceed the level of concern (RQ > 1).

Table 16 Ecoscenario Water Modelling EECs (µg a.i./L) in 80 cm and 15 cm Deep Water Body for Iprodione Use on Turf, Excluding Spray Drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
In a 80 cm Water Body for Use on turf ([illegible] at [illegible] intervals)						
BC Fraser Valley	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
MB Winnipeg	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ON Toronto	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
QC Montreal	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NS Greenwood	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
In a 15 cm Water Body for Use on turf ([illegible] at [illegible] intervals)						
BC Fraser Valley	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
MB Winnipeg	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
ON Toronto	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
QC Montreal	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
NS Greenwood	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Table 17 Ecoscenario Water Modelling EECs (µg a.i./L) in 80 cm and 15 cm Deep Water Body for Iprodione Use on Crops, Excluding Spray Drift

Crop and Use Pattern	Region	EEC (µg a.i./L)					
		Peak	96-hour	21-day	60-day	90-day	Yearly
In a 80 cm Water Body							
[illegible]	BC Fraser Valley	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	MB Winnipeg	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ON Toronto	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	QC Montreal	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	NS Greenwood	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
In a 15 cm Water Body							
[illegible]	BC Fraser Valley	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	MB Winnipeg	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	ON Toronto	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	QC Montreal	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	NS Greenwood	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Table 18 Low Rate Level 2 Estimated Environmental Concentrations (µg/L) of Iprodione and RP30228 in Potential Sources of Groundwater

	Turf 5760 + 2x1440 g a.i./ha at 14 days			Orchard 1x750g a.i./ha			Canola 1x374g a.i./ha		
	Daily	Yearly	50-yr avg	Daily	Yearly	50-yr avg	Daily	Yearly	50-yr avg
Iprodione	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
RP30228	185	184	130	16	16	11	7.2	7.2	5.0

Table 19 Runoff risk Assessment on Non-Target Aquatic Organisms Using Iprodione Runoff Values as Predicted by PRZM-EXAMS Model

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA* (µg a.i./L)	Use Scenario / EEC (µg a.i./L)	RQ	LOC exceeded
Freshwater organisms							
Freshwater Invertebrate	Acute	*Daphnia magna*	48-h LC$_{50}$ = 240	120	Turf - 123	**1.0**	Yes
					Crop - 59	0.5	No
	Chronic	*Daphnia magna*	21-d NOEC = 170	170	Turf - 30	0.2	No
					Crop - 19	0.1	No
Freshwater fish	Acute	Channel catfish (*Ictalurus punctatus*)	96 - h LC$_{50}$ = 3100	310	Turf - 84	0.3	No
					Crop - 43	0.1	No
	Chronic	Fathead minnow (*Pimephales promelas*)	34-d ELS NOEC = 260	260	Turf - 30	0.1	No
					Crop - 19	<0.1	No
Amphibians	Acute	Surrogate fish (*Ictalurus punctatus*)	96 - h LC$_{50}$ = 3100	310	Turf - 356	**1.1**	Yes
					Crop - 180	0.6	No
	Chronic	Surrogate fish (*Pimephales promelas*)	34-d ELS NOEC = 260	260	Turf - 108	0.4	Yes
					Crop - 70	0.3	No
Freshwater algae	Acute	Freshwater diatom (*Navicula pelliculosa*)	120-h EC$_{50}$ = 48	24	Turf - 84	**3.5**	Yes
					Crop - 43	**1.8**	Yes
Marine/estuarine organisms							
Invertebrate	Acute	Mysid shrimp (*M. bahia*)	96-h LC$_{50}$ = 680	340	Turf - 84	0.2	No
					Crop - 43	0.1	No
	Chronic	Mysid shrimp (*Mysidopsis bahia*	21-d NOEC = 3.5	3.5	Turf - 30	**8.6**	Yes

Organism	Exposure	Species	Endpoint reported (µg ai/L)	Endpoint for RA* (µg ai/L)	Use Scenario / EEC (µg ai/L)	RQ	LOC exceeded
					Crop - 19	**5.4**	Yes
Mollusc	Acute	Eatern Oysters *(Crassostrea virginica)*	96-h LC_{50} = 2300	1150	Turf - 84	<0.1	No
					Crop - 43	<0.1	No
Marine /estuarine fish	Acute	Sheepshead minnow *(Cyprinodon variegates)*	96-h LC_{50} = 7700	770	Turf - 84	0.1	No
					Crop - 43	<0.1	No
Marine algae	Acute	Marine diatom *(Skeletonema costatum)*	120-h LC_{50} = 330	165	Turf - 84	0.5	Yes
					Crop - 43	0.3	No

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50}, LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.
Risk quotients shown in bold exceed the level of concern (RQ > 1).

Appendix IX Monitoring Data

Water Monitoring Data

Canadian and U.S databases were searched for reported levels of iprodione and RP30228 in surface and ground water monitoring data. In Canada, very few monitoring data are available and RP 30228 was not monitored. Most of the available data for iprodione and RP 30228 are from U.S.A. In general, data for iprodione and RP 30228 are very sparse. The available monitoring data is categorized under two parts; ground and surface water.

Groundwater

Only one study conducted in California in 1998 monitored the residues of iprodione and RP 30228 in ground water. In that study, iprodione was not detected and RP 30228 was detected below the LOQ <0.025 µg/L in only one sample out of 239 water samples analyzed. The rest of the studies including the registrant sponsored study conducted in Suffolk County, New York, monitored either only iprodione or iprodione and 3, 5-DCA (a product identified to be of health concerns to the USEPA). There was no detection of iprodione. The sparseness of monitoring data deterred the determination of EECs for use in human health exposure assessment. Table 17 summarizes available groundwater monitoring data.

Surface water

Similar to groundwater, only one study monitored the residues of iprodione and RP 30228 in surface water. This study, sponsored by the registrant, was conducted in Florida, New Jersey and Illinois regions. These sites were selected because their source water (Community Water Systems) originates from watersheds in high iprodione use and sales areas. Raw and finished water samples were sampled over a period of three years. Detections of iprodione and RP 30228 were observed only in the sites from New Jersey. At the New Jersey site, out of 109 raw samples, iprodione was detected 31 times in three years; 22 times were above the LOQ with a peak concentration of 0.559 µg/L. RP30228 was detected 19 times in three years with 10 detections above the LOQ and a peak concentration of 0.309 µg/L. 3,5 – DCA was not detected above the LOQ in raw water samples in three years; only one detection occurred with a concentration less than the LOQ.

Iprodione was detected 10 times in 103 finished water samples in the three years with four detections above the LOQ ranging from 0.062 to 0.221 ug/L. Iprodione and RP30228 were detected at less than the LOQ, six and four times, respectively, in the three years. No 3,5 – DCA was detected in finished water. This study indicates that the occurrence of iprodione –related residues are sporadic and very low in concentration (less than 1 ug/L). The results of the surface water monitoring study are summarized in Table 18.

Table 1 Summary of Available Iprodione, Iso-iprodione and 3,5-DCA Ground Water Monitoring Data in Canada and United States and Norway

Data					Iprodione			Iso-iprodione			3,5-DCA		
	Source	Water Type	Period	Total # of samples	# detected	Max. detected (µg/L)	Average (including ½ LOD)	# detected	Max. detected (µg/L)	Average (including ½ LOD)	# detected	Max. detected (µg/L)	Average (including ½ LOD)
Canada	Alberta	Treated	1995-2003	13	-	-							
	Fraser Valley, B.C	Ground water	1992-1993	74	-								
U.S.A													
NAWQA	Wisconsin, Michigan	Ground water	2002-2007	70	-	-							
	30 states in United States	Ground water	2002-2007	2650	-	-							
RPAC	California	Ground water	1998	239	-	-	-	1	0.023		1	0.059	
Bayer sponsored	Suffolk county, New York	Bottled Water	1999-2007	21	-	-	-				-	-	-
		Community water systems		2937	-	- -	-				-	-	-
		Distribution		14	-	-	-				-	-	-
		Monitoring		183	-	-	-				-	-	-
		Non-Community water system		2464	-	-	-				-	-	-
		Private		6760	-	-	-				-	-	-
Norway		Shallow ground water	2007	450	-	-	-						

Table 2 Summary of Available Iprodione, Iso-iprodione and 3,5-DCA Surface Water Monitoring Data in Canada and the United States

Data					Iprodione			Iso-iprodione			3,5-DCA		
	Source	Water Type	Period	Total # of samples	# detected	Max. detected (µg/L)	Average (including ½ LOD)	# detected	Max. detected (µg/L)	Average (including ½ LOD)	# detected	Max. detected (µg/L)	Average (including ½ LOD)
Canada	Alberta	Surface	1995-2003	631	14	0.365							
		Treated	1995-2003	298	-								
U.S.A													
NAWQA	Wisconsin	Surface	2002-2007	169	3	0.05							
	30 states in United States	Surface	2002-2007	3557	69	0.30							
Bayer sponsored	Illinois	Raw surface	2006-2009	165	3	0.04	0.03	-					
		Treated		2	-	-	0.013	-					
	New Jersey	Raw surface		109	31	0.559	0.129	19	0.309	0.067	1	0.27	0.02
		Treated		103	10	0.221	0.06	4	0.049	0.03	-	-	
	Florida	Raw surface		161	-	-							
		Treated		4	-	-	-	-	-	-	-	-	-
PDP	California New York	Finished	2001	154	-	-	-	-	-	-	-	-	-
	CA, NY, Colorado, Kansas and Texas	Finished	2002	317	-	-	-	-	-	-	-	-	-

References

Chemistry

Studies/Information submitted by the registrant

PMRA Document Number	Reference
1450990	2006, Physical and Chemical Characteristics: Color, Physical Characteristics, Odor, Stability to Normal and Elevated Temperatures, metals and metal ions, pH, UV/visible Absorption, Melting point, Bulk Density, Partition Coefficient, Solubility, DACO: 2.14
1586699	1996, Iprodione - RP 26019: Product Identity and Composition, DACO: 2.13.1
1586702	1995, Technical Iprodione: Analysis and Certification of Product Ingredients, DACO: 2.13.1
1586636	Chemistry data used to support a Technical class product. IPD-RAH-1 June-September 1986, DACO: 2.99
1586629	Chemistry data used to support a Technical class product. IPD-RAH-1 1983-1985, DACO: 2.99

Toxicology

Studies/Information submitted by the registrant

PMRA Document Number	Reference
1128941	RP 26019 TECHNICAL ACUTE INHALATION TOXICITY- FOUR HOUR LC50 IN RATS (IPRODIONE)(RNP-75/775,378414), DACO: 4.2.3
1128942	PRIMARY SKIN IRRITATION STUDY IN RABBITS WITH IPRODIONE FINAL REPORT (3147.108), DACO: 4.2.5
1128943	IPRODIONE TECHNICAL-DERMAL SENSITIZATION TEST IN THE GUINEA PIG (BUEHLER METHOD)(209821/MRD-87-098), DACO: 4.2.6
1128945	21-DAY DERMAL TOXICITY STUDY IN RABBITS WITH IPRODINE TECHNICAL FINAL REPORT (3147.107), DACO: 4.3.4
1147787	POTENTIAL TUMORIGENIC AND TOXIC EFFECTS IN PROLONGED DIETARY ADMINISTRATION TO CD RATS FOR 104 WEEKS (69,93/042,RNP546/920) TOXICOLOGY REPORT SUMMARY (IPRODIONE), DACO: 4.4.2
1147788	POTENTIAL TUMORIGENIC EFFECTS IN PROLONGED DIETARY ADMINISTRATION IN MICE (70,93/054,RNP559/921240) TOXICOLOGY REPORT SUMMARY (IPRODIONE), DACO: 4.4.2

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1826554	Selim, S. (2003b) Determination of Permethrin (PER) and Piperonyl Butoxide (PBO) Residue on the Hand Following Hand Press on Treated and Untreated Vinyl and Carpet. Unpublished study prepared by Non-Dietary Exposure Task Force. (MRID 46188628). NDETF
1826562	Selim, S. (2004) Measurement of Transfer of Deltamethrin Residues from Vinyl and Carpet flooring Treated with a Fogger Formulation Following a Single Hand Press. Unpublished study prepared by Non-Dietary Exposure Task Force. (MRID 46297602). NDETF

Environment

A. Studies/Information submitted by the registrant

PMRA Document Number	**Reference**
1182248	Anaerobic aquatic metabolism of iprodione, W.C. Spare, completed December 18, 1990 (1510) [Rovral flo fungicide;subn.#97-1825 and 97-1826;regn.#24378 and 18977;submitted November 1997;volume 2 of 3], DACO: 8.2.3.5.6
1182249	A STUDY TO INVESTIGATE THE LEACHING OF 26 019 R.P. IN SOIL USING 14C-LABELLED 26 019 R.P., J.M. GOUOT ET AL., OCTOBER 8, 1976 (18845-E) [ROVRAL FLO FUNGICIDE;SUBN.#97-1825 AND 97-1826;REGN.#24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 2 OF 3], DACO: 8.2.4.3.2
1182263	Iprodione: adsorption/desorption to and from four soils and an aquatic sediment, C. M. Burr and S.E. Newby., completed June 28, 1994 (p94/014) [Rovral flo fungicide;subn.#97-1825 and 97-1826;regn.#24378 and 18977;submitted November 1997;volume 2 of 3], DACO 8.2.4.2
1182268	Iprodione: age leaching study in four soils, S.E. Newby et al, completed July 21, 1994 (p94/013) [Rovral flo fungicide;subn.#97-1825 and 97-1826;regn.#24378 and 18977;submitted November 1997;volume 2 of 3], DACO: 8.2.4.3.2
1182269	Iprodione-14C: aged leaching study with four soils, M.L. Doble et al, completed May 1991 (p91/050) [Rovral flo fungicide;subn.#97-1825 and 97-1826;regn.#24378 and 18977;submitted November 1997;volume 2 of 3], DACO: 8.2.4.3.2
1183191	HYDROLYSIS OF [PHENYL(U)-14C] IPRODIONE IN AQUEOUS SOLUTIONS BUFFERED AT PH 5, 7 AND 9, Y.T. DAS, COMPLETED DECEMBER 31, 1990 (89100;EC-89-050) [ROVRAL FLO FUNGICIDE;SUBN.#97-1825 AND 97-1826;REGN.#24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 1 OF 3], DACO: 8.2.3.2

1183199 AMENDMENT - FUNGICIDES: 14C-IPRODIONE: SOIL PHOTOLYSIS, A.E. JOHN ET AL., COMPLETED JULY 15, 1993 AND AUGUST 13, 1993 (P93/073;200287;4888) [ROVRAL FLO FUNGICIDE;SUBN #97-1825 AND 97-1826;REGN #24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 1 OF 3], DACO: 8.2.3.3.1

1183202 14C-iprodione aqueous photolysis, P.P. Adrian and J-M. Robles, completed April 19, 1991 (90-22;ag/crld/an/9115524) [Rovral flo fungicide;subn #97-1825 and 97-1826;regn #24378 and 18977;submitted November 1997;volume 1 of 3], DACO: 8.2.3.3.2

1183207 (14C)-iprodione: aerobic soil metabolism, A.R. Waring, completed December 20, 1993 (68/132;68/132-1015) [Rovral flo fungicide;subn #97-1825 and 97-1826;regn #24378 and 18977;submitted November 1997;volume 1 of 3], DACO: 8.2.3.4.2

1183210 DEGRADATION OF RP 26019 IN THE SOIL TREATMENT AT 1 AND 10 PPM WITH PHENYL 14C LABELLED MATERIAL, J.M. GOUOT ET AL., OCTOBER 11, 19977 (RP/RD/CNG AND CNG AN NO. 19320E) [ROVRAL FLO FUNGICIDE;SUBN #97-1825 AND 97-1826;REGN #24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 1 OF 3], DACO: 8.2.3.4.2

1183211 DEGRADATION OF RP 26019 IN THE SOIL 2 AND 5 PPM TREATMENTS WITH 14C LABELLED PRODUCT, GOUOT, LACROIX AND SAULL, AUGUST 31, 1976 (R.P./R.D./C.N.G. NO 18785) [ROVRAL FLO FUNGICIDE;SUBN #97-1825 AND 97-1826;REGN #24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 1 OF 3], DACO: 8.2.3.4.2

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1183215 Aerobic aquatic metabolism of iprodione, W.C. Spare, completed June 18, 1991 (1514) [Rovral flo fungicide;subn #97-1825 and 97-1826;regn #24378 and 18977;submitted November 1997;volume 2 of 3], DACO: 8.2.3.5.4

1183269 A LABORATORY DETERMINATION OF THE TOPICAL AND ORAL LD50S FOR HONEY BEES EXPOSED TO TECHNICAL-GRADE IPRODIONE, M. MEAD-BRIGGS, OCTOBER 24, 1995 (RP-95-5) [ROVRAL FLO FUNGICIDE;SUBN #97-1825 AND 97-1826;REGN #24378 AND 18977;SUBMITTED NOVEMBER 1997;VOLUME 1 OF 1], DACO: 9.2.4.1,9.2.4.2

1220782 Toxicity of iprodione (Rovral) to earthworms under field conditions & springtails under lab conditions, DACO: 9.2.3.1,9.2.7

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1759501 1993, (14C)-Iprodione: Aerobic soil metabolism, DACO: 8.2.3.4.2

1759502 1998, (14C)-RP 030228: Rate of degradation in three soil types under aerobic conditions, DACO: 8.2.3.4.2,8.2.3.5.2

1759503 1993, RP 30228: Adsorption to soil particles in three soil types, DACO: 8.2.4.2

1759504 1999, Iprodione metabolite: 14C-3,5-dichloroaniline - Soil adsorption/desorption study, DACO: 8.2.4.2

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1759512 2001, Field soil dissipation study in Europe Iprodione, DACO: 8.3.2.3

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1759523 1999, Effects on reproduction and growth of earthworms (*Eisenia andrei*) in artificial soil RP30228, DACO: 9.2.3.1

1759524 1999, Iprodione - effects on reproduction and growth of earthworms (*Eisenia andrei*) in artificial soil, DACO: 9.2.3.1

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1759526 1992, The acute toxicity of iprodione to earthworms (*Eisenia fetida*), DACO: 9.2.3.1

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1759542 1978, The acute toxicity of RP26019 technical assay 95.06% lot #77103-01 to the rainbow trout *Salmo gairdneri* Richardson, DACO: 9.5.2.1

1759543 1993, Acute toxicity study in the rainbow trout with RP 30228 (flow-through system), DACO: 9.5.2.1

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1759549	1988, The toxicity of iprodione technical to fathead minnow (*Pimephales promelas*) embryos and larvae, DACO: 9.5.3.1
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1759557	1981, One-generation reproduction - Mallard duck - Iprodione technical, DACO: 9.6.3.2
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1759560	1990, Iprodione technical - Toxicity to the freshwater diatom *Navicula pelliculosa*, DACO: 9.8.2
1759563	1995, *Scenedesmus subspicatus*, fresh water algal growth inhibition test with RP 30228, DACO: 9.8.2
1759564	1990, Iprodione technical - Toxicity to the freshwater bluegreen alga *Anabaena Flos-aquae*, DACO: 9.8.2
1759565	1995, *Scenedesmus subspicatus*, fresh water algal growth inhibition test with EXP10611 suspension concentrate at 225g/l (EXP10611), DACO: 9.8.2
1759566	1990, Iprodione technical - toxicity to the freshwater green alga *Selenastrum capricornutum*, DACO: 9.8.2
1759568	1991, Toxicity to the marine diatom *Skeletonema costatum* Iprodione technical Amended final report, DACO: 9.8.3
1759569	2002, Duckweed (*Lemna gibba G3*) growth inhibition test Iprodione substance, technical Code: AE F062470 00 1C96 0001, DACO: 9.8.5
1759570	1990, Iprodione technical - Toxicity to the duckweed Lemna gibba G3, DACO: 9.8.5
1785531	2000, Iprodione Metabolite: 14C-3,5-Dichloroaniline Aerobic Soil Metabolism, DACO: 8.2.3.4.2
1711132	1976, Acute toxicity of Rovral (26019RP) II. Oral, intraperitoneal and subcutaneous administration in mice, DACO: 4.2.1
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1711129	1976, Acute toxicity in rats, RP 26019, DACO: 4.2.1
1711116	1976, 30 228 R.P. : Acute toxicity and local tolerance , DACO: 4.2.1
1711136	1979, Iprodione (26019R.P.) one month toxicity study in mice by dietary administration , DACO: 4.3.3
1611932	1980, Iprodione sub-acute toxicity to mice by dietary administration for 13 weeks, DACO: 4.3.1
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1711135	1978, Three-month dietary oral toxicity study of 26 019 RP in rats, DACO: 4.3.1
1711117	1997, Iprodione 90-day study in the rat by dietary administration, DACO: 4.3.1
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B. Additional Information Considered

i) Published Information

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1311142	Byrtus Gary, et al, Alberta Environment, 2004, Alberta Environment, environmental assurance service, A summary of pesticide residues from the Alberta treated water survey, 1995 - 2003., DACO: 8.6
1311143	Byrtus Gary, et al, 2004, Alberta Environment, Environmental Assurance service, A summary of pesticide residues from the Alberta treated water survey, 1995 - 2003. raw data, DACO: 8.6
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1719719	US Geological Survey, 2009, Iprodione USGS NAWAQ surface water monitoring for iprodione (R61593) downloaded Feb 10 2009, DACO: 8.6
1794743	US EPA, 1998, Reregistration Eligibility Decision (RED) Iprodione, DACO: 12.5
1794745	European Commission - Health and Consumer Protection Directorate-General, 2002, Review report for the active substance Iprodione, DACO: 12.5
1794746	Leistra, Minze and Arrienne M. Matser, 2004, Adsorption, Transformation, and Bioavailability of the Fungicides Carbendazim and Iprodione in Soil, Alone and in Combination - Journal of Environmental Science and Health Part B - Pesticides, Food Contaminants
1794747	Stromqvist, Johan and Nicolas Jarvis, 2005, Sorption, degradation and leaching of the fungicide iprodione in a golf green under Scandinavian conditions: measurements, modelling and risk assessment - Pest Management Science, Vol. 61: 11687-1178, DACO: 8.6
1810595	Board for the Authorisation of Plant Protection Products and Biocides (CTGB, Netherlands), 2005, Reregistration decision for Rovral Aquaflo (Iprodione), DACO: 12.5.8,12.5.9
1816255	Iprodione (Pesticide residues in food: 1993 evaluations Part II Toxicology) Joint Meeting on Pesticide Residues, 1992, DACO: 12.5.4
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ii) Unpublished Information

PMRA Document Number	Reference
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Value

Additional Information Considered

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